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ERYTHROBLASTOSIS NEONATORUM

An Obstetrical-Pathological Study of 47 Cases

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ERYTHROBLASTOSIS neonatorum, or fetalis, has become a term used in the current literature when referring to hydrops fetalis, icterus gravis, and congenital anemia of the newborn, although Appleberg-Ulfspärre, Arnold and Downey, prefer the original terminology. These diseases of the fetus have in common a varying degree of erythroblastemia and erythroblastosis which is most marked in the hydrops variety. When immature white cells are numerous, the term erythroleucoblastosis is sometimes used, and in the earlier reports of both Jakesch and Klebs in 1878, and of Sanger in 1888, the condition was called fetal leucemia.

Hydrops fetalis has been recognized for centuries according to Ballantyne, who in 1898 collected 70 cases from the literature since 1614. The hematological picture was added by Schridde in 1910, and Rautman named the disease erythroblastosis in 1912. Icterus of the newborn has also been observed for centuries, but it remained for Blomfield in 1901 to differentiate physiological jaundice from icterus gravis. Even as late as 1908 Pfannenstiel held that icterus gravis was an intensification of physiological jaundice. The familial nature

of icterus gravis was noted by Buchan and Comrie, and they also called attention to the large numbers of nucleated red cells in the circulating blood as well as to the hematopoiesis in the liver and spleen. Ultimately, icterus gravis was included in the syndrome of erythroblastosis, and the subsequent reports of von Gierke, Yllpo, de Lange and Arntzenius, and others have substantiated this relationship. Although anemia is seen secondary to or associated with hydrops and icterus, congenital anemia *per se* was correlated with erythroblastosis neonatorum by Ecklin in 1919, with confirmatory reports by Susstrunk, Abt, and others. However, Hellman and Hertig regard the anemia only as a secondary manifestation of icterus gravis, to this we take exception, because of our own experience with 3 cases, as well as the reports in the literature. The occurrence of anemia and hydrops in infants of the same family as reported by Passachoff and Wilson, and anemia and icterus as reported by Diamond, Blackfan and Baty, may be regarded as further evidence that anemia is a separate entity.

It is often difficult to classify a given case of erythroblastosis fetalis into the hydropic, icteric, or anemic types because of the overlapping of symptoms. However, the prominent clinical feature is selected when designating

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livered infants with universal edema. The average parity was 3.2 and 3.1 for the two groups in contrast to 5.2 and 3 in the series of Hellman and Hertig.

Duration of gestation. The average was 36.3 weeks for the hydrops group and 39 weeks for the icterus group, showing that the former were born 1 month or more prematurely. In Capon's series of hydrops cases, the average duration was 33 weeks.

Complications of pregnancy. Capon, Hellman and Hertig, Darrow, and others state that the mother shows no characteristic pathognomonic signs. This may be true, but developments do occur during pregnancy and labor that should arouse suspicion, especially in the hydrops form of erythroblastosis, and include excessive uterine enlargement ("hydramnios") in 50 per cent, and toxemia of pregnancy in 31 per cent of the hydrops cases. Premature separation of the placenta, jaundice, and diabetes were present in several mothers.

Uterine enlargement out of proportion to the duration of pregnancy was frequently diagnosed as "hydramnios" clinically, and it has been so designated in the literature. The excessive uterine enlargement was found to be due to the combined weight of the placenta and infant, which in the hydrops cases averaged 4,674 grams, or 10.2 pounds. This is considerable for an average period of gestation of only 36 weeks. Figure 1 shows the placenta and infant of Case 1 which together weighed 4,950 grams, 10.7 pounds, the period of gestation was only 33 weeks. The edema of the infants makes them weigh more, so that they may be regarded as mature on the basis of weight when actually they are premature.

The incidence of toxemia of pregnancy was increased in both types of erythroblastosis, but was highest in the hydrops cases. Schumann found that 62 per cent of the cases reviewed by him had albuminuria and edema. Others, including de Lange, and Hellman and Hertig, found a high incidence of toxemia. Williamson and Vecchi have each reported a case of hydrops associated with postpartum eclampsia, and because of the rarity of such reports we record our own at this time.

CASE 1. Mrs. S. H., aged 27 years, Irish, parity 2-0-1-1,¹ who was delivered 3 years previously of an infant which died of icterus gravis. The Wassermann reaction was negative. The present pregnancy was complicated by an excessive weight gain of 25 kilograms, 55 pounds, by the thirty-second week of gestation. At this time an oliguria developed with

¹The patient has had 2 full term, 0 premature deliveries, 1 abortion and has 1 living child. Same explanation holds for Cases 3-6.



Fig. 1. Case 1. Macerated fetus with hydrops type of erythroblastosis, weight, 2,750 grams at 33 weeks' gestation, weight of placenta, 2,200 grams. From Stander, H. J. *Williams Obstetrics*, 8th ed., 1941.

3 plus albumin in the urine, the blood pressure rising to 165/110 and remaining at that level. She received the routine treatment for pre-eclampsia, including intravenous glucose. The nonprotein nitrogen rose from 29.2 milligrams per 100 cubic centimeters to 50.8, the uric acid from 5.6 milligrams to 7.6 milligrams, the carbon dioxide combining power decreased from 32.9 to 27.7 volumes per cent. Polyhydramnios was suspected clinically because of the excessive uterine enlargement. Roentgenographic studies were, therefore, conducted in order to determine the presence of soft tissue edema or abnormality of the fetus, since erythroblastosis was suspected. No halo or corona was seen about the fetal head, but, within the uterus, the infant had a Buddha-like habitus caused by the enlarged abdomen (Fig. 10b).

An induction of labor using castor oil, quinine, and an enema was successful, and, during the first stage of labor, the fetal heart was lost. The patient was delivered by breech extraction after a 7 hour labor. There was a postpartum hemorrhage of 700 cubic centimeters, which was attributed in part to the large placenta weighing 2,200 grams. It and the infant, which weighed 2,750 grams, had a combined weight of 4,950 grams, 10.2 pounds. Both are shown in Figure 1. The infant should have weighed about 1,600 grams for this period of gestation. Because of the postpartum hemorrhage, a blood transfusion was given to the mother. Three hours after delivery the mother developed two convulsive seizures. At this time she was given oxygen and molar lactate solution. Sixteen hours later, the nonprotein nitrogen had risen to 85.4 and the uric acid on the third postpartum day was 12.3 milligrams. Kidney function tests postpartum revealed a urea clearance of 73.5 per cent in 2 hours.

erythroblastosis as to type. During the course of this study we have observed 3 cases which had hemorrhagic diathesis as the first outstanding clinical sign. Such association is illustrated by Case 3. There were 3 other infants in our study that had erythroblastosis and erythroblastemia without clinical by drops, icterus, anemia, or hemorrhagic diathesis. They probably died before any of these complications had time to develop since 2 died before delivery. Two of these cases were proved by autopsy while the third was too badly macerated for histological interpretation, but the cord blood was sufficiently well preserved to give the diagnosis. References were also obtained in the literature to reports of erythroblastosis without hydrops, icterus, or anemia by Salomonsen de Lange and Ferguson.

A classification of erythroblastosis neonatorum based on our experience with 47 cases and substantiated by reports in the literature is presented: erythroblastosis with hydrops, 16 cases; erythroblastosis with icterus, 22 cases; erythroblastosis with anemia, 3 cases; erythroblastosis with hemorrhagic diathesis, 3 cases; erythroblastosis without hydrops, icterus, anemia, or hemorrhagic diathesis (*unclassified*) 3 cases.

Such a classification has academic value in clarifying our knowledge of the disease. It also has practical value since the infant mortality rate varies with the different types of the disease, as will be shown subsequently.

INCIDENCE

The incidence of erythroblastosis varies according to the type of the disease. The hydrops infants have

incidence of 348 in our material, and 3800 in the series of Wolf and Veigus. The icterus form in our series was 376 as compared to 500 found by Hellman and Hertig. This wide range is presumably due to a failure to recognize and diagnose the cases as has been our experience in the years 1933 to

1935 we observed only 7 cases in 39 premature and full term deliveries, or 1.75%. During the period 1936 to 1940, we have had 40 cases in 7520 deliveries, or .53%, an increase of nearly 400 per cent during the period of the present study.

Erythroblastosis is not frequently encountered yet one must be acquainted with it for

A 4th case of the milder form of erythroblastosis has been observed recently both by mother and previous infants with icterus gravis.

definite reasons. The incidence is 100 per cent for the mother that bears one of these infants, particularly when the baby dies, as so many of them do. Erythroblastosis is responsible for 3.2 per cent of our fetal deaths. The doctor-patient relationship may become strained if an infant with erythroblastosis is delivered by cesarean section as in cases reported by A. F. Abt (Smyth case), Bonney and Morton, and Pallas. A knowledge of this disease is necessary in making a differential diagnosis of other diseases of the newborn. It is noted that the medical examiners of the New York State Board asked a question on erythroblastosis in the examination on obstetrics in 1938. Finally, a research physician need feel no chagrin if his efforts bring knowledge and understanding of a disease even though much cannot be done from the standpoint of prevention and treatment. Prophylactic antepartum therapy for the child, for which Ballantyne first raised a plea, may be shown to have a practical application in erythroblastosis as it has in syphilis, and to that end, this study is dedicated.

MATERNAL DATA

Most of the following data have been obtained from 16 mothers bearing infants with hydrops, and 22 with icterus gravis. Inclusion of anemic, hemorrhagic and unclassified types would be somewhat controversial and their number is too small anyway to be statistically important so they have not been tabulated except when stated.

Age. The average maternal age was 33 and 30 years for the hydrops and icterus groups respectively. Hellman and Hertig have recorded similar ages for the 2 groups.

Race. It is generally believed that erythroblastosis is seen more frequently in patients having Mediterranean ancestry while Ott reports a high incidence

in the Scandinavian race. In our material nearly all of the races attending clinic were represented. However, proportion to the line population, 30 per cent were Irish in contrast to 4.5 per cent for the clinic and 9 per cent are negroes, versus 6.6 per cent for the clinic show a higher incidence in the Irish and negro race.

Parity. Of the total group of 47 mothers, there were only 3 primiparas, making multiparity decided factor 9 per cent of the patients. Potter reports 38 cases all in multiparas, and many others state that the first born escapes the disease. Schumann found 3 primiparas in 30 mothers that de-

livered infants with universal edema. The average parity was 3.2 and 3.1 for the two groups in contrast to 5.2 and 3 in the series of Hellman and Hertig.

Duration of gestation. The average was 36.3 weeks for the hydrops group and 39 weeks for the icterus group, showing that the former were born 1 month or more prematurely. In Capon's series of hydrops cases, the average duration was 33 weeks.

Complications of pregnancy. Capon, Hellman and Hertig, Darrow, and others state that the mother shows no characteristic pathognomonic signs. This may be true, but developments do occur during pregnancy and labor that should arouse suspicion, especially in the hydrops form of erythroblastosis, and include excessive uterine enlargement ("hydramnios") in 50 per cent, and toxemia of pregnancy in 31 per cent of the hydrops cases. Premature separation of the placenta, jaundice, and diabetes were present in several mothers.

Uterine enlargement out of proportion to the duration of pregnancy was frequently diagnosed as "hydramnios" clinically, and it has been so designated in the literature. The excessive uterine enlargement was found to be due to the combined weight of the placenta and infant, which in the hydrops cases averaged 4,674 grams, or 10.2 pounds. This is considerable for an average period of gestation of only 36 weeks. Figure 1 shows the placenta and infant of Case 1 which together weighed 4,950 grams, 10.7 pounds, the period of gestation was only 33 weeks. The edema of the infants makes them weigh more, so that they may be regarded as mature on the basis of weight when actually they are premature.

The incidence of toxemia of pregnancy was increased in both types of erythroblastosis, but was highest in the hydrops cases. Schumann found that 62 per cent of the cases reviewed by him had albuminuria and edema. Others, including de Lange, and Hellman and Hertig, found a high incidence of toxemia. Williamson and Vecchi have each reported a case of hydrops associated with postpartum eclampsia, and because of the rarity of such reports we record our own at this time.

CASE 1. Mrs. S. H., aged 27 years, Irish, parity 2-0-1-1,¹ who was delivered 3 years previously of an infant which died of icterus gravis. The Wassermann reaction was negative. The present pregnancy was complicated by an excessive weight gain of 25 kilograms (55 pounds), by the thirty-second week of gestation. At this time an oliguria developed with

¹The patient has had 2 full term, 0 premature deliveries, 1 abortion and has 1 living child. Same explanation holds for Cases 3-6.



Fig. 1. Case 1. Macerated fetus with hydrops type of erythroblastosis, weight, 2,750 grams at 33 weeks' gestation, weight of placenta, 2,200 grams. From Stander, H. J. *Williams Obstetrics*, 8th ed., 1947.

3 plus albumin in the urine, the blood pressure rising to 165/110 and remaining at that level. She received the routine treatment for pre-eclampsia, including intravenous glucose. The nonprotein nitrogen rose from 29.2 milligrams per 100 cubic centimeters to 50.8, the uric acid from 5.6 milligrams to 7.6 milligrams, the carbon dioxide combining power decreased from 32.9 to 27.7 volumes per cent. Polyhydramnios was suspected clinically because of the excessive uterine enlargement. Roentgenographic studies were, therefore, conducted in order to determine the presence of soft tissue edema or abnormality of the fetus, since erythroblastosis was suspected. No halo or corona was seen about the fetal head, but, within the uterus, the infant had a Buddha-like habitus caused by the enlarged abdomen (Fig. 10b).

An induction of labor using castor oil, quinine, and an enema was successful, and, during the first stage of labor, the fetal heart was lost. The patient was delivered by breech extraction after a 7 hour labor. There was a postpartum hemorrhage of 700 cubic centimeters, which was attributed in part to the large placenta weighing 2,200 grams. It and the infant, which weighed 2,750 grams, had a combined weight of 4,950 grams, 10.2 pounds. Both are shown in Figure 1. The infant should have weighed about 1,600 grams for this period of gestation. Because of the postpartum hemorrhage, a blood transfusion was given to the mother. Three hours after delivery the mother developed two convulsive seizures. At this time she was given oxygen and molar lactate solution. Sixteen hours later, the nonprotein nitrogen had risen to 85.4 and the uric acid on the third postpartum day was 12.3 milligrams. Kidney function tests postpartum revealed a urea clearance of 73.5 per cent in 2 hours.

erythroblastosis as to type. During the course of this study we have observed 3 cases which had hemorrhagic diathesis as the first outstanding clinical sign. Such association is illustrated by Case 3. There were 3 other infants in our study that had erythroblastosis and erythroblastemia without clinical hydrops, icterus, anemia or hemorrhagic diathesis. They probably died before any of these complications had time to develop since 2 died before delivery. Two of these cases were proved by autopsy while the third was too badly macerated for histological interpretation but the cord blood was sufficiently well preserved to give the diagnosis. References were also obtained in the literature to reports of erythroblastosis without hydrops, icterus or anemia by Salomonsen, de Lange and Ferguson.

A classification of erythroblastosis neonatorum based on our experience with 47 cases and substantiated by reports in the literature is presented: erythroblastosis with hydrops, 16 cases; erythroblastosis with icterus, 22 cases; erythroblastosis with anemia, 3 cases; erythroblastosis with hemorrhagic diathesis, 3 cases; erythroblastosis without hydrops, icterus, anemia or hemorrhagic diathesis (*unclassified*) 3 cases.

Such a classification has academic value in clarifying our knowledge of the disease. It also has practical value since the infant mortality rate varies with the different types of the disease as will be shown subsequently.

INCIDENCE

The incidence of erythroblastosis varies according to the type of the disease. The hydrops infants have an incidence of 348 in our material, and 3800 in the series of Wolf and Neigam. The icterus form in our series was 376 as compared to 500 found by Hellman and Hertig. This wide range is presumably due to failure to recognize and diagnose the cases as has been our experience. In the years 1933 to 1935 we observed only 7 cases in 1,089 premature and full term deliveries, or .64 per cent. During the period 1936 to 1940 we have had 40 cases in 17,530 deliveries, or .23 per cent, an increase of nearly 400 per cent during the period of the present study!

Erythroblastosis is not frequently encountered yet one must be acquainted with it for

A 24th case of the unclassified type of erythroblastosis has been observed recently born to a mother who had previous infants with (large group).

definite reasons. The incidence is 100 per cent for the mother that bears one of these infants, particularly when the baby dies, as so many of them do. Erythroblastosis is responsible for 3.2 per cent of our fetal deaths. The doctor-patient relationship may become strained if an infant with erythroblastosis is delivered by cesarean section, as in cases reported by A. F. Abt (Smyth's case), Bonney and Morton, and Pallos. A knowledge of this disease is necessary in making a differential diagnosis of other diseases of the newborn. It is noted that the medical examiners of the New York State Board asked a question on erythroblastosis in the examination on obstetrics in 1938. Finally a research physician need feel no chagrin if his efforts bring knowledge and understanding of a disease, even though much cannot be done from the standpoint of prevention and treatment. Prophylactic antepartum therapy for the child for which Ballantyne first raised a plea, may be shown to have a practical application in erythroblastosis as it has in syphilis, and to that end this study is dedicated.

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The first maternal prothrombin determination as done immediately postpartum. It was 68 per cent of normal, and on the following day it was 61 per cent. Thyloquinone was given (10 mgm) intramuscularly and on the third postpartum day the prothrombi was still 61 per cent, indicating probable failure of the liver to utilize the thyloquinone because of damage. This patient has been followed 18 intervals in the past 6 months and the prothrombin level is still considerably lower than normal. Further evidence of liver damage may be obtained from a study of the serum proteins during pregnancy for levels as low as 3.4 grams per 100 cubic centimeters were found.

Examination of the cord blood revealed 458 normoblasts and 87 erythroblasts per 100 white cells. The total white count was 50,000 of which 30,700 were nucleated red cells. The mean red cell diameter was 0. μ . There were many immature white cells in the smear. The hemoglobin was 11 per cent (gm Sahli) red blood corpuscles, 500,000 color index, 2.3 volume index, 5. The prothrombin and fibrinogen concentration of the cord blood were too low for determination—fetal death several hours previous. The serum proteins were also very low—9 grams per 100 cubic centimeters.

A autopsy revealed the characteristic pathology of the hydrops type of erythroblastosis. The liver was examined with interest because of the hydrops as well as the toxemia in the mother and it showed marked degeneration of the liver cords with associated postmortem changes.

Amniotic fluid. The color of the amniotic fluid has been described by many authors and the consensus is that it usually has a golden yellow color. In some of our cases, the color was often obscured by the passage of meconium resulting from fetal distress, which is frequently seen in erythroblastosis. A golden yellow amniotic fluid observed when the membranes rupture prematurely should arouse suspicion (See Case 6.)

Fetal distress while the fetus is alive. Auscultation of the fetal heart often revealed fetal distress which is indicative of intrauterine asphyxia. Sometimes the fetal heart as lost before the onset of or during labor. All the hydrops infants born alive and 50 per cent of the icterus infants required resuscitation by means of carbon-dioxide-oxygen mixture or the use of the Flagg apparatus. The fetal distress and systolic bruit were often helpful signs in making a correct antepartum diagnosis. The former also provided the indication for a large number of operative deliveries.

Operative incidence. In the hydrops group the operative incidence was 50 per cent, and in the icterus group (clinical per cent) 72 per cent. Two mothers were delivered by cesarean section was performed for premature separation of the placenta and the other because of 3 previous sections. Chief indication for operative interference (forceps) was fetal distress which occurred in 56 per cent.

Blood loss in the third stage of labor. The average blood loss in the hydrops group was 461 cubic centimeters which is greater than the average of 271 cubic centimeters for the clinical while the amount in the icterus group was not increased, namely 233 cubic centimeters. The increase in the hydrops group was caused by postpartum hemorrhage which occurred in 5 cases or 31 per cent, whereas only 1 case with icterus had a hemorrhage. The excessive bleeding in the hydrops group was caused by atony due to the overdistended uterus, large size of the placenta with an increased uterine surface to bleed, friability of the cotyledons with retained portions requiring manual removal as in one case and the factors associated with operative delivery.

Placenta. The average weight in the hydrops group was 341 grams the largest weighed 1,300 grams (Fig. 1). The average weight of the infants was 3,490 grams, giving an infant-placenta ratio of 3—normal 6:1. The average weight in the icterus cases was 603 grams the largest weighed 1,000 grams. The average weight of the infants in this group was 3,444 grams so that the normal ratio of 6:1 was obtained.

Inspection of the placentas of the infants with hydrops invariably revealed a pale maternal surface deeply fissured forming cotyledons which were friable. The fetal surface and membranes were stained yellow in 6 of our cases. In others, it was gray and glistening. On standing the placenta basin filled rapidly with a yellow colored serum so that in a short time the placenta lost as much as 500 grams in weight. The large size of the placenta is thought to be a response on the part of the fetal organism to faulty metabolism requiring an increase in the placental surface. The placenta of the icterus infants was of normal size as a rule there was little or no edema, the maternal surface had a normal red color with normal cotyledons the fetal membranes were discolored in 4 cases.

Previous to the present study begun in 1936 only 1 placenta had been saved for examination which has been the experience of most writers. However in the past 5 years we have examined 26 placentas, which will be reported elsewhere in greater detail. Suffice it to state for the present that the placentas of the hydrops cases bear a close resemblance to syphilis so that an erroneous diagnosis may be made. There is abnormal basophilia the villi are large and edematous with signs of immaturity as indicated by focal persistence of the Langhans layer and the presence of Hof-

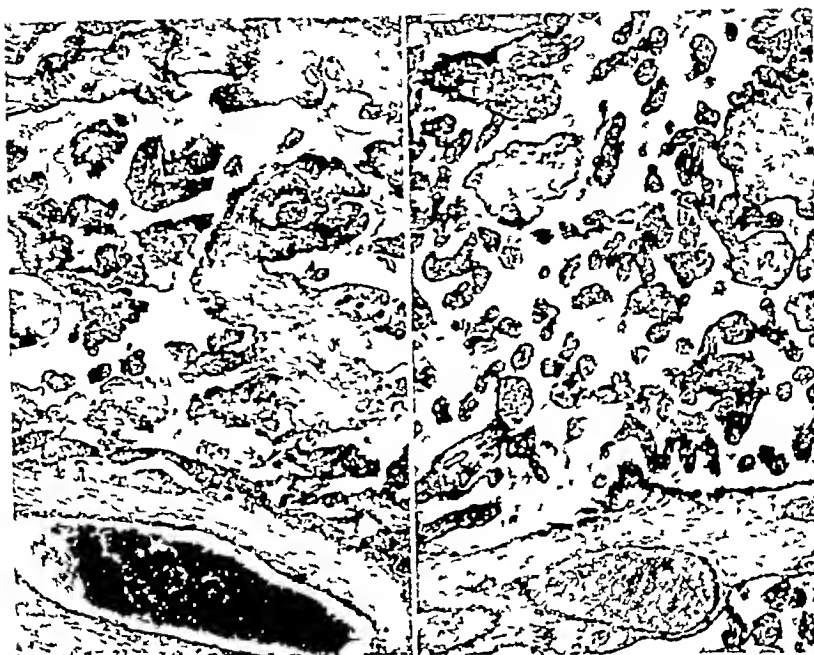


Fig 2 Photomicrographs of placentas in erythroblastosis Low power a, left, Hydrops case Note large, edematous, immature villi and fetal vessel filled with nucleated erythrocytes b, Icterus case Villi are more mature although some have edema Fetal vessel has fewer nucleated red cells

bauer cells (Fig 2a) The amnion and chorion often exhibit cells laden with a brownish pigment similar to that seen in the fetal liver and other organs The first histological report of the placenta was made by Goormaghtigh in 1927 He observed foci of hematopoiesis as have Hellman and Hertig We regard the immature red cells, erythroblasts and normoblasts in the fetal vessels of the placenta as of greater diagnostic value

The placentas of the icteric infants showed more mature villi although some showed slight edema The fetal vessels contained fewer normoblasts and occasional erythroblasts Basophilia was also less marked (Fig 2b)

Familial history This term is a misnomer A better designation would be "obstetrical history," or "maternal history," since the mother gives a history of bearing infants with the disease Her family history as well as that of the husband fails to reveal a similar tendency Erythroblastosis in repeated pregnancies has been reported by de Lange and many others

Erythroblastosis usually appears in the second or third, or even the fifth pregnancy, as a rule, although

primiparas may have infants with the disease When the first born has had erythroblastosis, it is very likely to recur in subsequent infants In the literature, Buhrman and Sanford, Commandeur, Diamond et al, Fleishmann and Wolff, Jatho, Zimmermann and Yannett, each report erythroblastosis in the first pregnancy with repetition in successive pregnancies Their cases together with 3 of our own have had a total of 27 pregnancies resulting in only 1 healthy infant without erythroblastosis

The occurrence of erythroblastosis in terms of total number of pregnancies was 34.2 per cent for the hydrops group, and 31.4 per cent in the icterus group These percentages are in close agreement with those of Macklin, 30 and 58 per cent, respectively The hydrops group had more abortions than the icterus group, as well as history of erythroblastosis in previous infants These mothers have no difficulty in becoming pregnant, which speaks for the normalcy of the ova and sperm

There were 131 pregnancies in the hydrops and icterus groups resulting in 43 infants with erythroblastosis These were studied as to the appearance of erythroblastosis, and it was found that the lowest incidence occurred in the first pregnancy and that the tendency increased with successive pregnancies The percentages were approximately the same for both the hydrops and icterus groups Recurrence of erythroblastosis after its first appearance is about 50 per cent for the hydrops group and 40 per cent

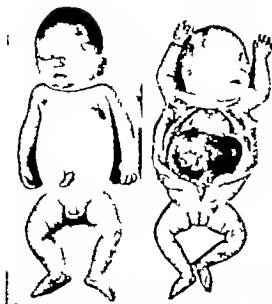


Fig. 3. Infants with hydrops type of erythroblastosis. a, left, Case 3. Child weighed 3,070 grams at 37 weeks gestation. Placenta weighed 800 grams. Pronounced nephritic fluid was separated from chest and abdomen as an aid to resuscitation. Death occurred 5 minutes after delivery by dissection to show enlarged heart, liver, and spleen. (From Wolfe, S. A., and Nelson, I. Am. J. Obst.)

for the icterus group. Hellman and Hertig report 50 and 80 per cent for the two groups respectively.

The delivery of normal infants after the appearance of erythroblastosis in the previous infant was observed in 4 patients (not primiparas). These infants had no special prenatal therapy nor was there a change in husbands. However these mothers had had normal infants prior to the appearance of erythroblastosis.

Multiple pregnancy. Erythroblastosis has been reported in twins by Woolley, Oberdorfer, MacAlhonn, Abt, Buhrman and Sanford, and Andrews and Miller. Veterinarians have observed the hydrops form in one of litter of pups. Sometimes one twin is normal, as in de Lange case. Blakely found in her survey of the literature that when one twin had hydrops, the other was normal in 8 out of 9 cases, whereas with icterus, both twins were so affected in 5 out of 7 cases. Unfortunately most of the reports fail to distinguish between identical or fraternal twins. This is of importance since erythroblastosis may be congenital disturbance affecting only one twin, as in MacAlhonn case of identical twins, whereas both of the monozygotic twins reported by Snyder and Ford had fetal hydrops.

Of our 47 cases, only one mother had single ovum twins (female), one of which was dead-born and macerated and had the unclassified type of erythroblastosis; the other died at the age of 3 days of congenital anemia, prematurity and cardiac hypertrophy. Other features of this case are as follows:

CASE. Mrs. E. T. Hungarian, 26 years old, primigravida, who had a seventh pregnancy, the diagnosis of twins having been confirmed by x-ray. The Wassermann was negative. Labor began spontaneously in the thirty-eighth week of gestation, and after 9-hour labor in A, weighing 50 grams, as delivered by breech extraction. It lived for 3 days and developed petechiae and convulsions. Examination of the cord blood at birth revealed a red corpuscle count of 3,500,000, hemoglobin 5 grams, the white cell count, 55,000 and 20 erythroblasts and 95 normoblasts per 100 white cells. The cord prothrombin was 7 per cent of normal, the fibrinogen was 25 grams per cent without evidence of hemorrhagic diathesis. During life 4 transfusions were given and 2 milligrams of synthetic vitamin K (thylloquinone Squibb). The infant died on the second day of life. The prime pathological features comprised large heart, eight to 30 grams, hepatomegaly of the liver and spleen, the areas of focal necrosis in the former.

Twin B was a dead-born and macerated female weighing 450 grams. A smear of cord blood showed 6 erythroblasts and 7 normoblasts per 100 white cells. The white cell count was 3,000. Since the blood was hemolyzed, no further studies were made. Autopsy revealed marked a toxemia so that histological diagnosis could not be carried out. The placenta weighed 800 grams and examination of the membranes confirmed the diagnosis of single ovum twins. Grossly the placenta revealed deeply stained membranes for twin B and histologically the outstanding criteria were the normoblasts in the fetal vessels.

The diagnosis of erythroblastosis of the unclassified type was made on twin B while twin A was considered as having the anemic form of the disease. It is probable that had twin B been born alive it might have developed anemia or icterus and could then have been classified in the conventional manner.

Blood studies. Fifteen mothers (7 hydrops) had complete hematological examination including smear, while the rest had a average of 1 or more hemoglobin determinations during the puerperium course. All were within normal limits, save for mild anemia cases Moore and Pastore has reported case of erythroblastic splenomegaly in mother who delivered normal infant. Doe reports the occurrence of erythroblastosis in the blood of

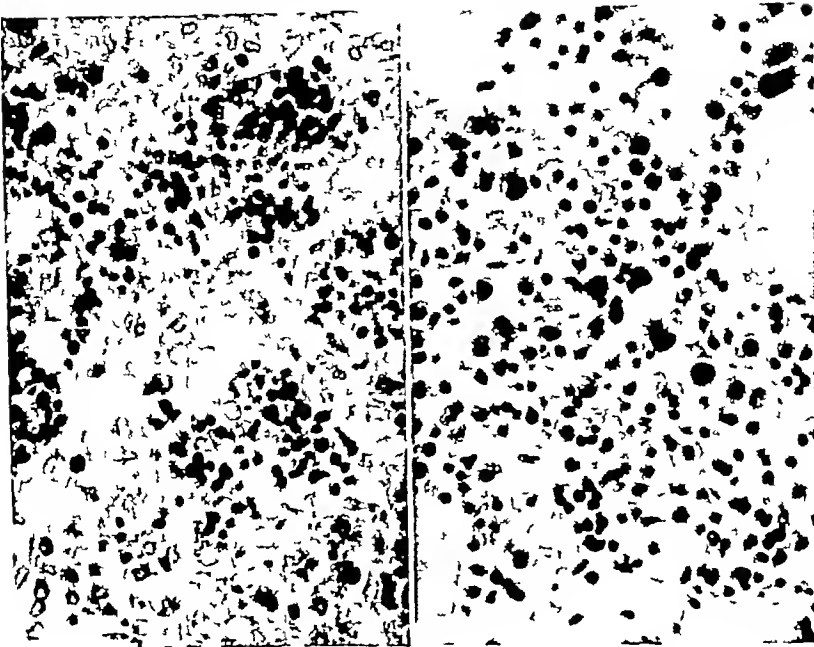


Fig 7 Photomicrographs of liver and bone marrow in hydrops type of erythroblastosis $\times 190$ a, left, Liver, showing hematopoietic foci and cellular degeneration b, Bone marrow showing marked hyperplasia of granular elements, numerous immature erythrocytes

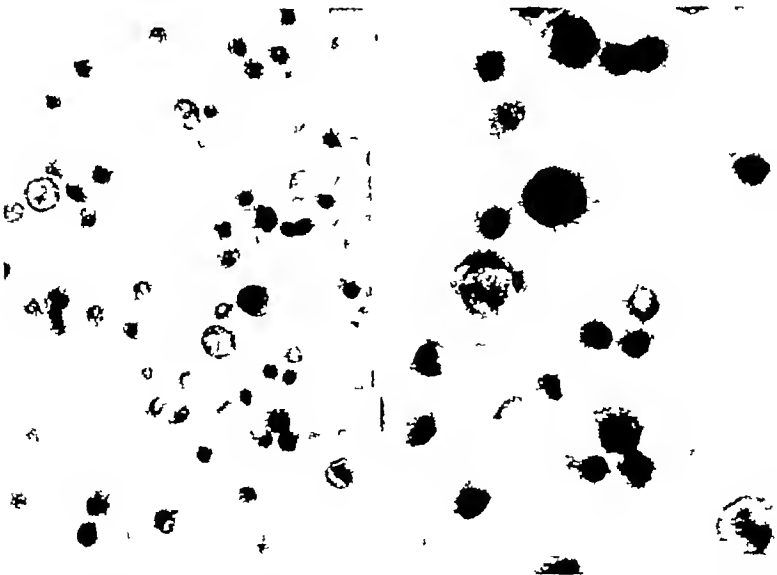


Fig 8 Photomicrographs of cord blood Low and high magnification Note large erythroblasts and smaller normoblasts (See Fig 9, frontispiece)

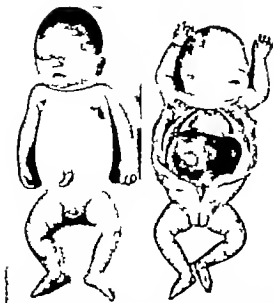


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average weight in the icterus group was 3,442 grams, which agrees with the duration of 39 weeks' gestation. There was 1 premature child in this group.

Appearance at birth The hydropic child has marked pitting edema, the neck is short, and there is a suggestion of Mongoloid facies. The abdominal and thoracic distention is due to effusion and a large liver, and may be so marked that the natural posture of the child is prevented, causing it to assume a Buddha-like position, as was sometimes observed *intra uterum* by x-ray (Fig 10b). The arms and legs seem shorter than normal and the skin is usually macerated if the child is stillborn, as many of them are (Figs 1 and 3a). The vernix may have a yellow color. The child with the icterus form of erythroblastosis is usually born alive and may or may not be slightly yellow at birth, or become so soon thereafter (Fig 4, frontispiece). The child may require resuscitation. Liver and spleen are usually enlarged.

Congenital anomalies Such defects were found in 10 of the 47 infants, or 21 per cent, and included harelip and cleft palate, spina bifida, hydrocele, supernumerary fingers, cervical rib, urethral stricture, and an interventricular septal defect. Murphy gives the incidence of congenital defects in deceased liveborn and stillborn infants as 0.54 and 0.68 per cent, respectively, so that the incidence in our infants with erythroblastosis is approximately 40 times greater. Weber and Scholtz have described a case of hydrops fetalis that had multiple congenital anomalies, Vecchi's case had polydactylia and cystic kidneys, and the case reported by Bourret and Lathoud also had cystic kidneys. Murphy found that families possessing two or more malformations had subsequent offspring with the same deformity in 50 per cent of the infants. This corresponds closely to our incidence of 50 and 40 per cent for the hydrops and icterus cases, respectively, and to the 50 per cent incidence reported by Macklin. It seems from this evidence that any theory must consider the congenital aspect when used to explain the pathogenesis of erythroblastosis, enzygotic twins sometimes have the disease, which is further evidence of its congenital nature.

Symptoms in addition to hydrops and icterus The clinical differentiation of erythroblastosis into hydrops, icterus, anemia, and hemorrhagic forms may be difficult because of an overlapping of signs. For instance, a baby with hydrops may develop jaundice (Case 4), and an icteric infant may develop focal edema about the eyelids and scrotum, while both of these types may also have an associated anemia. They may also show evidence of hemorrhagic diathesis as a coexisting complication, or it may be the first evidence *per se* of erythroblastosis, as in Case 3. Finally, a few infants may die *in utero* (Case 2), or may not live long enough to develop any of the usual signs of hydrops, icterus, or anemia. Nevertheless, they may have erythroblastosis as we have observed in 4 cases, and these have been placed in an *unclassified* group, and have already been referred to.

Of the 25 infants born alive and having erythroblastosis, the following clinical signs were observed: focal edema in 16 cases, pallor in 12, skin petechiae in 16, visceral hemorrhages in 7, 3 of which were thought to be hemorrhagic disease until blood studies showed the erythroblastosis, cyanosis in 17, dyspnea in 10, convulsions in 4. Many infants had two or more of these signs in addition to the hydrops or icterus. The high incidence of hemorrhagic diathesis, 29 per cent, and skin petechiae, 64 per cent, indicates an increased capillary permeability. The usual incidence of hemorrhagic disease of the newborn has been shown by Javert and others to be only 0.7 per cent.

The following case illustrates the occurrence of melena as the first indication of erythroblastosis. This case is important in that the mother subsequently delivered an infant with erythroblastosis associated with hemorrhagic diathesis, and previously had delivered an infant with hydrops fetalis.

CASE 3 Mrs P S, aged 33, negro, parity 9-8-1-6, delivered a deadborn, macerated and edematous infant in her previous pregnancy, the autopsy showed erythroblastosis. The present pregnancy was complicated by a mild pre-eclampsia. She was delivered in the thirty-eighth week of gestation, after a 2½ hour labor, by breech extraction. This baby weighed 3,820 grams. Soon after birth it developed dyspnea, skin petechiae, facial twitchings, and had a large bloody stool. The liver and spleen were enlarged. The red blood cell count on the first day of life was 4,300,000, hemoglobin, 16 grams, white blood cells, 38,100, 140 nucleated red cells were counted per 100 white cells. Two transfusions were given in addition to supportive therapy, but slight edema of the extremities occurred and the child died 36 hours after birth. The chief pathology comprised erythroblastosis of the liver and spleen, with many nucleated red cells in the vessels. There was subarachnoid and cerebellar hemorrhage to which death was attributed. The placenta weighed 880 grams and was grossly unremarkable.

Two years later, this mother was delivered of her ninth full term child in the thirty-seventh week of gestation. Again she had a mild pre-eclampsia. This child weighed 4,580 grams. On the first day of life the white blood cell count was 42,000 and there were 4 erythroblasts and 98 normoblasts per 100 white cells. The red count was 6,000,000 for which reason only serum transfusions were given. The child developed slight edema, cyanosis, and many skin petechiae of the face and arms. He made an uneventful recovery.

Essential autopsy data In general, the hydrops cases showed a greater degree of erythroblastosis and erythroblastemia than did the icterus types, as shown by 29 complete postmortem examinations (88 per cent).



Fig. Roentgenograms showing hydrops fetalis *in utero*. (Retouched) a, left, Fetal head has "balo" due to edema of scalp. b, Habitus of fetus conforms to "Buddha, or frog-like posture due to abdominal enlargement caused by ascites and large liver.

mothers with "pregnancy kidney and eclampsia. The Kline Wassermann reaction was negative in 11 of the 47 cases. There was not the slightest indication of syphilis which is of significance since the placenta was occasionally so diagnosed. The Rh⁺ agglutin of Levine and Katzin was absent in several mothers.

The blood chemical constituents were studied in 9 mothers with the following average results per 100 cubic centimeters of blood:

	Mothers with erythroblastosis	Control at term (Standard)
Kempton's astrogens	2 mgm.	48 mgm.
Urea-nitrogen	3.7 mgm.	mgm.
Uric acid	5 mgm.	5 mgm.
Chlorides	3.5 mgm.	46.4 mgm.
Sugar	5 mgm.	60 mgm.
Carbon dioxide combining power	35 vol. %	5 vol. %
Icterus index	5-9 units	0-3 units

The chief deviation from normal was seen in the blood uric acid and carbon dioxide combining power which was explained by the presence of toxemia in most of the mothers studied. The icterus index was not elevated, and ranged from 3 to 20 units in 7 mothers with hydrops, and ranged 5 units in 3 mothers having infants with icterus gravis (normal < 3 units). The icterus index of the cord blood of

Rh⁺ as antigen present in the red cells of all *Macaca* (rhesus monkeys) (since the normal, and in 100 cent of human blood, while 100 cent of the population at large is Rh negative. According to Levine (personal communication), 90 per cent of the mothers having infants with erythroblastosis are Rh negative. The blood of the fathers and the infants is usually Rh positive.

the infants was 9 units and 66 units for the two types, respectively (normal < 5 units). Ten mothers had clinical jaundice and Buhman and Sanford observed it in one of their cases in the last month of pregnancy. It is due either to diffusion of bilirubin from the infant through the placenta into the maternal circulation, or to the maternal liver dysfunction, or both of these factors.

The serum proteins were studied in 3 mothers and the average of determinations was 5.0 grams per 100 cubic centimeters which is below the normal for pregnant patient at term. Case had as little as 3.4 grams, and she delivered an infant with hydrops that had .9 grams per 100 cubic centimeters. Prothrombin determinations in which the technique of Warner, Brinkhaus and Smith were used, showed varying concentrations ranging from 20 to 100 per cent.

Mortality. All of the 47 mothers survived.

INFANTS DATA

These are presented for the most part on the basis of 16 cases of the hydrops and 22 cases of the icterus gravis types of erythroblastosis.

Sex. In the hydrops group, there were 9 males and 7 females, whereas in the icterus group there was a preponderance of males, 4 to 8.

Birth weight. The average weight of the hydrops group was 3,420 grams, which is .000 grams more than for the average of 36 weeks gestation. The

wood, Strong and Marks, and others have associated icterus gravis as a possible forerunner of hepatolenticular degeneration

The epiphyseal line was described as normal in some cases and widened in others, which may indicate metabolic disturbance. There were no histological or roentgenological evidences of syphilis. The bone marrow was hyperplastic and contained many immature cells of the red and white series in varying degrees of maturation (Fig 7b). The persistence of hematopoietic foci in the liver and organs as well as the bone marrow hyperplasia certainly indicate that there is no lack of antianemic principle required for red cell maturation. It is possible that the immature red cells enter the circulation from the foci located in the various organs and not only from the bone marrow.

Heart blood cultures These were obtained in 18 infants and were negative in all, confirming the studies of Abt, Diamond and his co workers, and ruling out sepsis neonatorum.

Cord blood studies These were made on 5 hydrops cases and 3 infants with icterus gravis, while 11 infants of the latter group were studied on the first day of life and are, therefore, comparable to the cord blood studies. The average of the findings are as follows:

	RCC	Hgb (gms)	CV	WCC	NRC	Index	Color
5 Hydrops cases	1.51	5.5	25	54.3	37.6	1.5	1.3
3 Icterus cases	3.50	14.7	52	47.0	21.2	1.3	1.4
11 Icterus cases on first day of life	3.1	13.6		37.2	18.5		1.4

Cord blood studies in erythroblastosis are seldom described in the literature. We have studied smears of cord blood in 9 cases of hydrops and 6 cases of icterus. The average results of these studies are:

	Normo- blasts	Erythro- blasts	Reticulo- cytes	Immature polymor- phous clear	Immature lympho- cytes	Red cell diam- eter
0 Hydrops	30.4	9.8	7.1%	34	16	0.54
0 Icterus	71	14		10	0	0.50

The hydrops cases showed marked macrocytosis and polychromasia, with numerous erythroblasts, normoblasts, mitotic figures, and reticulocytes (Fig 8). The immature polymorphonuclear cells were abundant as were lymphoblasts, which confirms the findings of Diamond, Blackfan, and Baty. The volume index (normal 1.08) and color index (normal 1.2) were very much increased in both groups. The mean corpuscular diameter (normal 8.5 μ) was not increased in the icterus group, but was markedly so in the hydrops infants (0.5 μ). The macrocytosis

suggests liver damage or insufficiency, for Kracke and Garver, and others find liver disease complicated by a macrocytic anemia. The ratio of normoblasts to erythroblasts in the hydrops group was 3.8:1, and 5:1 in the icterus group. In normal pre-mature infants, according to Javert, it is 6.6:1, and in full term infants 14:1.

The blood studies vary greatly with the clinical type of the disease. In the hydrops type, the red cell count may be as low as 500,000 per cubic millimeter. The nucleated red cells are acetic acid resistant and are, therefore, present in the counting chamber as "white cells," and may number up to 300,000 per cubic millimeter.

Smears stained by the Wright technique (Fig 9, frontispiece) reveal megalocytic erythroblasts with large nuclei containing a lacy chromatin network and several nucleoli, with a cytoplasm which is basophilic since hemoglobin is deficient or absent. Mitotic figures are frequent. The normoblasts are smaller and approach the red cell in size. They have a cytoplasm which is less basophilic, and the nuclei are smaller and pycnotic. The degree of erythroblastemia varies with the hydrops or icterus types, being more pronounced in the former.

The degree of erythroblastosis seems to control the severity of erythroblastemia, for in the hydrops type in which both are most pronounced, a great many immature red cells—erythroblasts—can be found in the circulating blood. In the icteric form, nucleated red cells are fewer in number and are more mature—normoblasts—while in the anemic form of the disease these cells are even more mature—reticulocytes and normoblasts. Consequently, it is probable that the hematopoietic foci as well as the hyperplastic bone marrow liberate these cells.

In the icterus cases that survived, there was a gradual decrease in the number of nucleated red cells so that in the first week to 10 days of life, they had virtually disappeared from the circulating blood. Therefore, the diagnosis had best be made hematologically at birth or soon thereafter, for it may be missed as in one of our cases in which a normal blood smear was made on the tenth day of life but autopsy revealed unmistakable evidence of erythroblastosis. The rate of disappearance may have prognostic value. Case 4, an infant with hy-

The chief deviation from normal, in addition to the hydrops or icterus, was seen in the heart, liver and spleen (Fig 3b). The heart was invariably hypertrophied, and in some cases weighed 40 grams. This hypertrophy caused fetal distress as well as cardiac murmurs, which were heard in 3 infants with icterus and 6 with hydrops and of the latter 3 were heard *intra utero*. Histological section of the heart muscle usually showed vacuolization due to the edematous infiltration.

The liver and spleen were invariably increased in weight and on histological examination numerous hematopoietic foci and sinusoids were seen filled with immature red and white cells (Fig 5 frontisplece). The foci were often more numerous in the hydrops cases, and have been regarded by Abt as a persistence of embryonal blood formation. Since these infants were more immature than the icterus gravis cases, we feel that prematurity may be sufficient to explain the difference. Deposits of pigment could be seen in the Kupffer and liver cells in the hydrops cases (Fig 6 frontisplece). The pigment is stained blue in some cells and remains brown in others. This may represent hemoglobin of fetal and adult origin as suggested by Darrow, Nowakovsky and Austin. The icterus cases usually had no intracellular pigment, but had instead numerous bile thrombi. The livers of several deadborn infants were so autolyzed that histological study was impossible yet the pigment was readily observed. Its presence may prove of diagnostic importance when tissues are extremely macerated. Many livers showed varying degrees of cloudy swelling, fatty degeneration, or necrosis (Fig 7a) and these changes together with the intracellular pigment and hematopoietic foci, which constituted from 10 to 40 per cent of the liver structure made up a liver parenchyma of greatly impaired functional capacity. Degeneration is observed in the livers of infants dying of other causes, but its presence in erythroblastosis, in addition to the hematopoietic foci and intracellular pigment, would speak for impaired hepatic function if the postmortem changes could be definitely ruled out. In general the histological changes were most marked in the hydrops group. De Lange

and Arntzenius found cases without degeneration of the liver as we have also observed while others, including Klemperer and Hawkey and Lightwood, have described the degenerative changes. Subsequent juvenile cirrhosis of the liver may be traceable to icterus gravis according to Boynton and Wyllie. Brink and Ebbs, while Wilson has associated hepatic degeneration with pathology of the lenticular nuclei. Cirrhosis of the liver may be associated with low serum proteins, edema and death, as reported in a 2½ year old girl by Thompson, Ziegler and McQuarrie. Hypoproteinemia has been regarded by Weech and others as the result of severe liver damage.

Hematopoiesis was usually evident in other organs including the kidney, adrenal, thymus, thyroid, pancreas, and various lymph nodes. The degree of involvement was greatest in the hydrops cases. The kidney sometimes showed cloudy swelling and tubular degeneration in addition to deposits of pigment, which may handicap the child after birth when excretion by the placental route is no longer present.

The serous cavities usually contained amber colored fluid in varying amounts, and this was most marked in the hydrops cases. The abdominal cavity at times contained up to 150 cubic centimeters of amber colored fluid.

Petechial hemorrhages were often seen in the internal organs which, together with the clinical evidence of skin petechiae and hemorrhage diathesis, may be attributed to impaired capillary permeability.

Kernicterus, first described by Schmidt, was observed in 5 or 45 per cent of the icterus cases and in none of the 9 hydrops cases that came to autopsy. The basal nuclei of the brain particularly the optic thalamus, olivary bodies and the dentate and lenticular nuclei were involved. Two of the 5 cases that showed the condition had convulsions with no sign of intracranial hemorrhage. Zimmerman and Yannett described a child of 3 years with a history of icterus gravis who had residual spasticity and mental retardation. Degeneration of the basal nuclei was found at autopsy and the possible relation to kernicterus was emphasized. The association of lenticular degeneration and liver cirrhosis was made by Wilson in 1912. Parsons, Hawkey and Light

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drops surviving 11 days, had 42 normoblasts per 100 white cells on the day of death.

Blood chemistry of fetus. The chemical constituents of the cord blood per 100 cubic centimeters is presented in the following table.

	Hydrops cases	Icterus cases	Control
Nonprotein nitrogen	(4) 41.7 mgm.	(3) 60 mgm.	33 mgm.
Uric acid	(3) 7.3 mgm.	(3) 3.8 mgm.	3 mgm.
Chlorides	(3) 503 mgm.	(3) 305.8 mgm.	500 mgm.
Serum proteins	(3) 3.6 gm.	(3) 6.3 gm.	5 gm.
Fibrinogen	(3) .07 gm.	(3) .07 gm.	.1 gm.
Prothrombin	(3) 5%	(3) 7%	5 gm.
Icterus index	(3) 91 units	(3) 64 units	18 units

(Figures in parentheses denote number of cases studied)

The increased values in the nonprotein nitrogen and uric acid may accompany the higher values observed in the mothers, caused by the pre-eclamptic type of toxemia. The chlorides were elevated in the hydrops group. The serum proteins were decreased in both the hydrops and icterus cases, but to greater extent in the former and in case were as low as .4 grams. The hypoproteinemia is thought to be the result of liver damage which was the greatest in the hydrops group. Weech has found lowered serum proteins following impairment of liver function in other conditions and in case of congenital syphilis.

The prothrombin concentration of the cord blood was studied in 7 cases of erythroblastosis and an average level of between 3 and 7 per cent of normal was obtained. The lowest values were observed in cases with hydrops. The Warner Briakhorn, and Smith test was employed and, as Jvert and Moore have shown, the prothrombin concentration of cord blood is normally about 3 per cent of the adult normal. The hypoprothrombinemia, the lowered serum proteins, the edema and hemorrhagic diathesis, all speak of impaired capillary permeability and may be associated with impaired liver function, being most marked in the hydrops cases.

Rh factor. Determinations made by Levin in 6 cases showed the cord blood to be Rh positive in all. The blood of the fathers and mothers were Rh positive and negative respectively with one exception which will be reported elsewhere.

Differential diagnosis. In addition to the classification of erythroblastosis neonatorum as to type, it is necessary to rule out the following conditions: approximate order of frequency physiological jaundice, prematurity, intracranial hemorrhage, hemorrhagic disease of the newborn, congenital heart disease, congenital syphilis, sepsis neonatorum, obliteration of the bile ducts, familial acholuric jaundice, Winckel disease and hypoproteinemia.

Treatment. In addition to the supportive measures such as oxygen infusions and artificial feedings repeated transfusions were given. As many as 9 transfusions, averaging 60 cubic centimeters in amount, were given in the first days of life. We agree with Arnold

and Downey who state that the physician who fails to give enough blood is able to make complete case reports including the autopsy protocol. Hampson has used intramuscular whole blood in icterus gravis with good results which Hawkinsley and Lightwood failed to duplicate. The value of whole blood by vein and intramuscularly in addition to the cellular elements may be due in part also to the protein and prothrombin content. For this reason vitamin K may be of value, and we have used it in several cases. The transfusions were given with blood from donors that were compatible. Since the blood of the infants is Rh positive tests for this factor may also be indicated.

Fetal mortality. In 1937 the author first directed attention to erythroblastosis as an important cause of fetal mortality, stating that it was 3 1/2 times greater than syphilis. It is responsible for more fetal deaths than asphyxia neonatorum, hemorrhagic disease of the newborn and toxemia of pregnancy. Macklin, Potter and others have since written on the rôle of erythroblastosis in infantile mortality. In a study of 750 fetal deaths in infants weighing over 1500 grams, including stillbirth and neonatal deaths up to the fourteenth day of life 3.3 per cent were caused by erythroblastosis and 1.3 per cent were due to syphilis. Syphilis as such has been overrated as a cause of stillbirths.

The fetal mortality rate in our 47 cases varied with the type of erythroblastosis encountered. Of this number 70 per cent perished.

Type of erythroblastosis	Still or dead-born	Non-fatal	Number of deaths Total	Percentage
Hydrops (8 cases)	—	7	16	100
Icterus (11 cases)	—	—	—	54
Asymptomatic (3 cases)	—	—	—	33
Hemorrhagic diathesis (3 cases)	—	—	—	33
Unclassified (3 cases)	—	—	3	100
Total	—	—	33	70

The mortality rate was 100 per cent in the hydrops cases although infant survived for period of days (Case 4). The rate for the icterus cases is about 50 per cent, which agrees with the observations of Hellman and Hertig. Of the unclassified cases, death was due to prolonged and intrapartum infection in cases like the third case as one of 1 has been reported (Case 5).

The following case is unusual in that the infant with hydrops fetalis survived 11 days. Wolfe and Neigus report 6 days, Hellman and Hertig 2 days, as the longest period of survival.

CASE 4 Mrs D T, aged 31 years, American Hebrew, parity 2-0-3-2, in whom two spontaneous abortions occurred between her first and last full term infants, which are alive and well. The present pregnancy was complicated by "hydramnios", the uterus measured 39 centimeters at term (41 weeks gestation). Delivery was effected with forceps, the indication for which was fetal distress in the second stage of labor. The baby was excessive in size, weighing 4,380 grams, part of which was due to subcutaneous edema. The child required simple resuscitation at birth. The placenta weighed 1,760 grams. No histological section was made. The amniotic fluid was described as greenish yellow. The mother sustained a blood loss in the third stage of 660 cubic centimeters, part of which was due to a laceration into the right broad ligament because of dystocia due to difficulty with the shoulders.

Because of the edema of the infant, hematological studies were made at once. The red count was 5,200,000 per cubic millimeter, hemoglobin, 14.6 grams, white count 6,400, of which 3,400 were nucleated red cells, 86 nucleated erythrocytes, including erythroblasts, were counted per 100 white cells. The bleeding and clotting times were normal. On the subsequent day the serum proteins were 5.0 grams per 100 cubic centimeters, the blood calcium was 11.6, phosphorus 6.5, cholesterol 131, urea nitrogen 33 milligrams, chlorides 591 milligrams per 100 cubic centimeters. On the third day of life, definite jaundice developed (icterus index 100) and the edema seemed to be increasing. Petechiae developed on the face, and attacks of dyspnea and cyanosis were frequent. In addition to the usual supportive measures, the child was given 8 transfusions (total 405 c cm citrated blood) and despite this, the red blood cell count was 4,900,000 and the hemoglobin 14 grams on the day of death. Nucleated red cells persisted in the blood stream and on the day of death there were 42 nucleated red cells per 100 white cells in the circulating blood. The nucleated cells disappear in 4 days in normal infants according to Javert and about 10 days in infants with erythroblastosis. The rate of disappearance may have prognostic significance.

Autopsy revealed the presence of greenish yellow fluid in the pericardial (7 c cm), pleural (10 c cm) and abdominal (50 c cm) cavities. The heart was enlarged, weighing 45 grams, the liver weighed 203 grams, the spleen 10 grams. The liver and spleen showed diffuse erythroblastosis, the liver having in addition, fatty degeneration and portal fibrosis. Hematopoietic foci were also seen in the adrenal and kidney. Petechial hemorrhages were observed in the heart, thymus, adrenal and lungs. The bone marrow showed erythroblastic and granulocytic hyperplasia. Blood culture and Kline reaction were negative.

ANTEPARTUM DIAGNOSIS

This study has been presented for the most part from the obstetrical point of view and only the pertinent pathological and pediatric features have been discussed. Our aim has been to feature certain criteria which may prove helpful in making a correct antepartum diagnosis. This has obvious importance in the obstetrical management of the mother. For instance, in Case 5 patient was very anxious for a cesarean section in order to give the child every opportunity for survival, for several physicians had so advised her. The presence of an infant with hydrops was proved and section was refused.

CASE 5 Mrs L H, aged 34 years, white, parity 2-0-2-0, with a history of two abortions and two previous infants with hydrops, was first seen in the twenty-eighth week of gestation. A hematological examination revealed a normocytic hypochromic anemia for which iron was prescribed. The serum proteins were reduced and averaged 5.2 grams per 100 cubic centimeters, the plasma fibrinogen was only 0.3 gram per 100 cubic centimeters, while the prothrombin was 100 per cent of normal. The patient was placed on a high protein diet, rich in vitamins.

In the thirty-fifth week of pregnancy, the height of the uterus measured 36 centimeters and "hydramnios" was suspected. At this time a fetal bruit became evident. The patient remarked that the fetal activity was not great. Ankle edema became a prominent sign and a low protein diet was ordered. There was a gain of 4 kilograms in the following week. The blood pressure, which had been normal previously, rose suddenly to 170/100 and remained at that level, while albuminuria developed. At this time, the patient was hospitalized for study and treatment. The blood chemical findings included a uric acid reading of 7.4 milligrams per 100 cubic centimeters and a carbon dioxide combining power of 36.2 volumes per cent. Intravenous glucose was given. An x-ray examination of the fetus was made, a soft tissue technique being used in order to show soft tissue edema. A suggestive halo was observed about the child's head. However, the Buddha or frog-like posture of the infant was found to be more definite (see Fig 10b).

In the meantime, the maternal blood pressure increased to 180/110, the albuminuria persisted although the edema improved. In view of the toxemia and the increased hazard to the infant, the patient and her husband clamored for delivery by cesarean section. However, by this time sufficient data had been collected, namely, obstetrical history, hydramnios, fetal heart murmur, toxemia, and x-ray evidence of edema in the infant, all of which pointed to a diagnosis of erythroblastosis fetalis of the

drops surviving 11 days, had 43 normoblasts per 100 white cells on the day of death.

Blood chemistry of the fetus. The chemical constituents of the cord blood per 100 cubic centimeters is presented in the following table:

	Hydrops cases	Icterus cases	Control
Nonprotein nitrogen	(4) 41.7 mgm.	(1) 60 mgm.	35 mgm.
Uric acid	(4) 7.5 mgm.	(1) 1.5 mgm.	3 mgm.
Chlorides	(4) 503 mgm.	(1) 201.0 mgm.	500 mgm.
Serum proteins	(4) 3.5 gm.	(1) 1.3 gm.	3.4 gm.
Fibrinogen	(4) 0.4 gm.	(1) 0.3 gm.	1 gm.
Prothrombin	(4) 5%	(1) 7%	1 gm.
Icterus index	(7) 97 units	(1) 64 units	1 gm.

(Figures in parentheses denote number of cases studied)

The increased values in the nonprotein nitrogen and uric acid may accompany the higher values observed in the mothers, caused by the pre-eclamptic type of toxemia. The chlorides are elevated in the hydrops group. The serum proteins were decreased in both the hydrops and icterus cases, but to a greater extent in the former and in 1 case were as low as 1.4 grams. The hypoproteinemia is thought to be the result of liver damage which was the greatest in the hydrops group. Weech has found lowered serum proteins following impairment of liver function in other conditions, and in a case of congenital syphilis.

The prothrombin concentration of the cord blood was studied in 7 cases of erythroblastosis and an average level of between 3 and 7 per cent of normal as obtained. The lowest values were observed in cases with hydrops. The Warner, Brinkhous and Smith test was employed and, as of Wert and Moore have shown, the prothrombin concentration of cord blood is normally about 3 per cent of the adult normal. The hypoprothrombinemia, the lowered serum proteins, the edema and hemorrhagic diathesis, all speak for impaired capillary permeability and may be associated with impaired liver function, being most marked in the hydrops cases.

Rh factor. Determinations made by Levin in 6 cases showed the cord blood to be Rh positive in all. The blood of the fathers and mothers were Rh positive and negative respectively with one exception which will be reported elsewhere.

Differential diagnosis. In addition to the classification of erythroblastosis neonatorum as 1 type, it is necessary to rule out the following conditions in approximate order of frequency: physiological jaundice, prematurity, intracranial hemorrhage, hemorrhagic disease of the newborn, congenital heart disease, congenital syphilis, sepsis neonatorum, obstruction of the bile ducts, familial cholemic jaundice, Winkler disease and hypoproteinemia.

Treatment. In addition to the supportive measures such as oxygen infusions and artificial feedings repeated transfusions were given. As many as 9 transfusions, averaging 60 cubic centimeters in amount were given in the first days of life. We agree with Arnold

and Downey who state that the physician who fails to give enough blood is able to make complete case reports including the autopsy protocol. Hampson has used intramuscular whole blood in icterus gravis with good results which Hawkeley and Lightwood failed to duplicate. The value of whole blood by vein and intramuscularly in addition to the cellular elements may be due in part also to the protein and prothrombin content. For this reason vitamin K may be of value, and we have used it in several cases. The transfusions were given with blood from donors that were compatible. Since the blood of the infants is Rh positive tests for this factor may also be indicated.

Fetal mortality. In 1937 the author first directed attention to erythroblastosis as an important cause of fetal mortality stating that it was 2½ times greater than syphilis. It is responsible for more fetal deaths than asphyxia neonatorum, hemorrhagic disease of the newborn, and toxemia of pregnancy. Macklin, Potter and others have since written on the rôle of erythroblastosis in infantile mortality. In a study of 750 fetal deaths in infants weighing over 1500 grams, including stillbirth and neonatal deaths up to the fourteenth day of life, 3.2 per cent were caused by erythroblastosis and 1.3 per cent were due to syphilis. Syphilis as such has been overrated as a cause of stillbirths.

The fetal mortality rate in our 47 cases varied with the type of erythroblastosis encountered. Of this number 70 per cent perished.

Type of erythroblastosis	Still or dead before birth	Number of deaths	Percent
		Total	Age
Hydrops (18 cases)	—	6	100
Icterus (1 case)	—	1	100
Anemia (5 cases)	—	3	100
Hemorrhagic diathesis (3 cases)	—	3	100
Unclassified (3 cases)	—	3	100
Total	—	13	70

The mortality rate was 60 per cent in the hydrops cases although all survived the period of 15 days (Case 4). The rate for the icterus cases is about 50 per cent, which agrees with the observations of Hoffman and Hertig. Of the unclassified cases death was due to prolapsed cord and intraperitoneal infection in cases while the third case as one of them were reported (Case 5).

The following case is unusual in that the infant with hydrops fetalis survived 11 days. Wolfe and Neigus report 6 days, Hellman and Hertig 2 days, as the longest period of survival.

CASE 4 Mrs D T, aged 31 years, American Hebrew, parity 2-0-3-2, in whom two spontaneous abortions occurred between her first and last full term infants, which are alive and well. The present pregnancy was complicated by "hydramnios", the uterus measured 39 centimeters at term (41 weeks gestation). Delivery was effected with forceps, the indication for which was fetal distress in the second stage of labor. The baby was excessive in size, weighing 4,380 grams, part of which was due to subcutaneous edema. The child required simple resuscitation at birth. The placenta weighed 1,760 grams. No histological section was made. The amniotic fluid was described as greenish yellow. The mother sustained a blood loss in the third stage of 660 cubic centimeters, part of which was due to a laceration into the right broad ligament because of dystocia due to difficulty with the shoulders.

Because of the edema of the infant, hematological studies were made at once. The red count was 5,200,000 per cubic millimeter, hemoglobin, 14.6 grams, white count 6,400, of which 3,400 were nucleated red cells, 86 nucleated erythrocytes, including erythroblasts, were counted per 100 white cells. The bleeding and clotting times were normal. On the subsequent day the serum proteins were 5.0 grams per 100 cubic centimeters, the blood calcium was 11.6, phosphorus 6.5, cholesterol 131, urea nitrogen 33 milligrams, chlorides 591 milligrams per 100 cubic centimeters. On the third day of life, definite jaundice developed (icterus index 100) and the edema seemed to be increasing. Petechiae developed on the face, and attacks of dyspnea and cyanosis were frequent. In addition to the usual supportive measures, the child was given 8 transfusions (total 405 c cm citrated blood) and despite this, the red blood cell count was 4,900,000 and the hemoglobin 14 grams on the day of death. Nucleated red cells persisted in the blood stream and on the day of death there were 42 nucleated red cells per 100 white cells in the circulating blood. The nucleated cells disappear in 4 days in normal infants according to Javert and about 10 days in infants with erythroblastosis. The rate of disappearance may have prognostic significance.

Autopsy revealed the presence of greenish yellow fluid in the pericardial (7 c cm), pleural (10 c cm) and abdominal (50 c cm) cavities. The heart was enlarged, weighing 45 grams, the liver weighed 203 grams, the spleen 10 grams. The liver and spleen showed diffuse erythroblastosis, the liver having in addition, fatty degeneration and portal fibrosis. Hematopoietic foci were also seen in the adrenal and kidney. Petechial hemorrhages were observed in the heart, thymus, adrenal and lungs. The bone marrow showed erythroblastic and granulocytic hyperplasia. Blood culture and Kline reaction were negative.

ANTEPARTUM DIAGNOSIS

This study has been presented for the most part from the obstetrical point of view and only the pertinent pathological and pediatric features have been discussed. Our aim has been to feature certain criteria which may prove helpful in making a correct antepartum diagnosis. This has obvious importance in the obstetrical management of the mother. For instance, in Case 5 patient was very anxious for a cesarean section in order to give the child every opportunity for survival, for several physicians had so advised her. The presence of an infant with hydrops was proved and section was refused.

CASE 5 Mrs L H, aged 34 years, white, parity 2-0-2-0, with a history of two abortions and two previous infants with hydrops, was first seen in the twenty-eighth week of gestation. A hematological examination revealed a normocytic hypochromic anemia for which iron was prescribed. The serum proteins were reduced and averaged 5.2 grams per 100 cubic centimeters, the plasma fibrinogen was only 0.3 gram per 100 cubic centimeters, while the prothrombin was 100 per cent of normal. The patient was placed on a high protein diet, rich in vitamins.

In the thirty-fifth week of pregnancy, the height of the uterus measured 36 centimeters and "hydramnios" was suspected. At this time a fetal bruit became evident. The patient remarked that the fetal activity was not great. Ankle edema became a prominent sign and a low protein diet was ordered. There was a gain of 4 kilograms in the following week. The blood pressure, which had been normal previously, rose suddenly to 170/100 and remained at that level, while albuminuria developed. At this time, the patient was hospitalized for study and treatment. The blood chemical findings included a uric acid reading of 7.4 milligrams per 100 cubic centimeters and a carbon dioxide combining power of 36.2 volumes per cent. Intravenous glucose was given. An x-ray examination of the fetus was made, a soft tissue technique being used in order to show soft tissue edema. A suggestive halo was observed about the child's head. However, the Buddha or frog-like posture of the infant was found to be more definite (see Fig 10b).

In the meantime, the maternal blood pressure increased to 180/110, the albuminuria persisted although the edema improved. In view of the toxemia and the increased hazard to the infant, the patient and her husband clamored for delivery by cesarean section. However, by this time sufficient data had been collected, namely, obstetrical history, hydramnios, fetal heart murmur, toxemia, and x-ray evidence of edema in the infant, all of which pointed to a diagnosis of erythroblastosis fetalis of the

drops surviving 11 days, had 42 normoblasts per 100 white cells on the day of death.

Blood chemistry of the fetus. The chemical constituents of the cord blood per 100 cubic centimeters is presented in the following table:

	Hydrops cases	Icterus cases	Control
Nonprotein nitrogen	(4) 41.7 mgms.	(1) 60 mgms.	35 mgms.
Uric acid	(1) 7.5 mgms.	(1) 3.5 mgms.	2.1 mgms.
Chlorides	(1) 284 mgms.	(1) 265.0 mgms.	300 mgms.
Serum proteins	(1) 3.8 gm.	(1) 5.2 gm.	2 gm.
Fibrinogen	(1) .04 gm.	(1) 0.2 gm.	1 gm.
Prothrombin	(1) 5%	(1) 7%	1 gm.
Icterus index	(1) 91 units	(1) 66 units	1 unit

(Figures in parentheses denote number of cases studied)

The increased values in the nonprotein nitrogen and uric acid may accompany the higher values observed in the mothers caused by the pre-eclamptic type of toxemia. The chlorides are elevated in the hydrops group. The serum proteins were decreased in both the hydrops and icterus cases, but to a greater extent in the former and in case were as low as 1.4 grams. The hypoproteïnemia is thought to be the result of liver damage which was the greatest in the hydrops group. Wetch has found lowered serum proteins following impairment of liver function in other conditions, and in case of congenital syphilis.

The prothrombin concentration of the cord blood was studied in 7 cases of erythroblastosis and average level of between 3 and 7 per cent of normal as obtained. The lowest values are observed in cases with hydrops. The Warner, Briakhouse, and Smith test was employed and, as Jervet and Moore have shown, the prothrombin concentration of cord blood is normally about 3 per cent of the adult normal. The hypoprothrombinemia, the lowered serum proteins, the edema and hemorrhagic diathesis, all speak for impaired capillary permeability and may be associated with impaired liver function, being most marked in the hydrops cases.

Rh factor. Determinations made by Levine in 6 cases showed the cord blood to be Rh positive in all. The blood of the fathers and mothers were Rh positive and negative respectively, with one exception which will be reported elsewhere.

Differential diagnosis. In addition to the classification of erythroblastosis neonatorum as 1 type, it is necessary to rule out the following conditions in approximate order of frequency: physiological jaundice, prematurity, intracranial hemorrhage, hemorrhagic disease of the newborn, congenital heart disease, congenital syphilis, sepsis neonatorum, obliteration of the bile ducts, familial acholuric jaundice, Winkler disease and hypoproteïnemia.

Treatment. In addition to the supportive measures such as oxygen infusions and artificial feedings repeated transfusions were given. As many as 9 transfusions averaging 60 cubic centimeters in amount, were given in the first days of life. We agree with Arnold

and Downey who state that the physician who fails to give enough blood is able to make complete case reports including the autopsy protocol. Hampson has used intramuscular whole blood in icterus gravis with good results which Hawkeley and Lightwood failed to duplicate. The value of whole blood by vein and intramuscularly in addition to the cellular elements may be due in part also to the protein and prothrombin content. For this reason vitamin K may be of value and we have used it in several cases. The transfusions were given with blood from donors that were compatible. Since the blood of the infants is Rh positive tests for this factor may also be indicated.

Fetal mortality. In 1937 the author first directed attention to erythroblastosis as an important cause of fetal mortality stating that it was 25 times greater than syphilis. It is responsible for more fetal deaths than asphyxia neonatorum, hemorrhagic disease of the newborn and toxemia of pregnancy. Macklin, Potter and others have since written on the role of erythroblastosis in infantile mortality. In a study of 750 fetal deaths in infants weighing over 1500 grams, including stillbirth and neonatal deaths up to the fourteenth day of life, 32 per cent were caused by erythroblastosis and 13 per cent were due to syphilis. Syphilis as such has been overrated as a cause of stillbirths.

The fetal mortality rate in our 47 cases varied with the type of erythroblastosis encountered. Of this number 70 per cent perished.

Type of erythroblastosis	Still or dead-born	Neonatal	Total	Percentage
Hydrops (6 cases)	—	—	6	100
Icterus (1 case)	—	—	1	100
Anemia (3 cases)	—	—	3	100
Hemorrhagic diathesis (3 cases)	—	—	3	100
Unclassified (1 case)	—	—	1	100
Total	—	—	14	70

The mortality rate was 100 per cent in the hydrops cases although 1 infant survived for a period of 11 days (Case 4). The rate for the icterus cases is about 50 per cent, which agrees with the observations of Hellman and Hertig. Of the anemic cases, death was due to prolonged cord and intrapartum infection in 2 cases, while the third case was one of twins here reported (Case 7).

hydrops type. The parents request for cesarean section was refused. Instead, the membranes were ruptured artificially (the uterus being very irritable) and after short labor of 6 hours, midforceps delivery was effected with the pediatrician in attendance. The placenta was very large and edematous with a pale maternal surface, very friable, and was delivered with difficulty because of its large size (100 grams). A blood loss of 500 cubic centimeters was sustained in the third stage of labor. Postpartum course was uncomplicated.

The child weighed 3,020 grams (excessive for 37 weeks gestation) part of which was due to marked generalized edema. It lived for 3 minutes during which time resuscitation with carbon-dioxide-oxygen mixture was carried out. Fluid was also aspirated from the thorax and abdomen to remove these obstacles to respiration, and blood was obtained from the cord for cross matching and blood studies. The red cell count was 1,000,000 per cubic millimeter hemoglobin 3 per cent (Sahlb) white cell count 9,600 per cubic millimeter of which 6,93 were nucleated red cells. The red cell volume was 3 millimeters per cent. The volume index was 6 and the color index .5 and the mean corpuscular diameter was 0.7μ . In the stained smear 3 normoblasts and 3 erythroblasts were counted per 100 hlt cells. Many of the latter were immature, and 6 per cent of the red cells were reticulocytes. The plasma prothrombin was less than 5 per cent of normal, the serum proteins were only .45 grams, and the nonprotein nitrogen was 4.7 and the chloride 7.8 milligrams per 100 cubic centimeters. The uterus index was 75 cts. Autopsy and histological examination confirmed the diagnosis of erythroblastosis fetalis.

This patient became pregnant 6 months later and a therapeutic abortion was performed because of residual renal and liver damage following the severe pre-eclampsia. The history of 3 infants with erythroblastosis may have contributed to the decision to terminate the pregnancy although it was not used as the indication. At this time studies of the Rh factor revealed the mother to be negative and the father to be positive. The patient has since adopted a child. This case also illustrates the gloomy obstetrical future of primiparas having a firstborn infant with erythroblastosis as discussed above under Familial History.

There are cases that have a normal course until labor begins and then developments occur such as loss of fetal movement, irregular fetal heart, premature rupture of the membranes with escape of yellow fluid, etc., which should arouse suspicion. Diagnosis at this

stage of pregnancy is illustrated by the following case referred to in the preliminary report of this study made in 1937.

CASE 6. Mrs. N. J. was a 29 year old Armenian woman, parity 0-0-1 with a negative Wassermann. The pregnancy was uneventful until the thirty-eighth week of gestation when the membranes ruptured prematurely and it was observed that the fluid had a golden yellow color. The head was dipping well into the pelvis the cervix was closed and there were no uterine contractions. The fetal heart was slow with a rate of 60 to 80 per minute. As contractions developed, the rate increased. However rectal ether without quinine was given in order to relax the uterus between pains. Spontaneous delivery occurred after labor of 9 hours.

The infant was a female weighing 3,341 grams. The vernix had a golden yellow color and the child had a suggestive Mongoloid appearance. There was localized edema of the eyelids. Resuscitation with carbon-dioxide-oxygen mixture was necessary. The cord blood was promptly studied and 80 normoblasts and 20 erythroblasts were counted for 100 white cells. The red count was 5,600,000 and the hlt count 80,000 of which 20,000 were nucleated red cells. Despite prompt diagnosis and transfusion of 60 cubic centimeters of compatible blood, the infant died 3 hours after delivery. Autopsy confirmed the clinical diagnosis. The placenta weighed 660 grams, had marked yellow color of the membranes, and histologically was remarkable only in that the nucleated red cells were increased in the fetal vessels.

A correct antepartum diagnosis of erythroblastosis neonatorum was made correctly by the author in 8 out of 10 cases. The signs having the greatest value in the 10 cases in which intrauterine diagnosis was attempted are as follows: multiparity 10 cases excessive uterine enlargement (hydramnios) 6 amniotic fluid, yellow-brown, 6 premature labor 6 nationality (Irish) 6 uterus index increased, 5 erythroblastosis in a previous infant, 4 toxemia of pregnancy 4 fetal distress before or during labor 3 intrauterine death of the fetus, 3 systolic bruit of fetal heart heard in the uterus, 3 aspiration of cord blood before delivery (prolapsed cord) 1 x-ray examination of fetus while within the uterus (7 cases studied) 2.

To recapitulate, multiparity and excessive uterine enlargement beyond the duration of gestation were valuable criteria, while the previous obstetrical history was less important. The x-ray was found to be among the

JAVERT ERYTHROBLASTOSIS NEONATORUM

least valuable aids Its use is limited to the hydrops cases We took our first roentgenogram in May, 1936, in an effort to detect edema of the scalp It was not successful Subsequently, we have studied 7 cases, 2 proved to have infants with icterus, and 5 with hydrops The edema of the scalp, or so called "halo," as reported by Hellman and Irving in 938, was seen in only 2 hydrops cases (see Fig 10a) However, these and other cases showed a Buddha or frog-like habitus of the child which may be attributed to the enlarged fetal abdomen and hydrothorax (Fig 10b) The roentgenogram in another case revealed a very large placenta The large placenta together with fetal movements within the uterus makes roentgenological demonstration of the "halo" and fetal habitus rather difficult We have come to place greater reliance on the Buddha position and recommend anteroposterior and lateral plates to show the posture of the child in suspected hydrops cases Antepartum diagnosis may be facilitated by maternal and paternal blood studies for the Rh factor if the results are interpreted with the history and clinical data presented

PATERNAL STUDIES

In a recent report, Otto stated that 5 cows serviced by the same bull had 5 hydropic calves When sired by a different bull, the same cows delivered normal calves With this information in mind, 6 fathers of infants with erythroblastosis (4 hydrops and 2 icterus) were studied The semen examination revealed a total average volume of 3.7 cubic centimeters with an average of 88 per cent normal sperm, which compares favorably with the values for healthy males as stated by Cary, who made these studies The genitalia were not abnormal One father had a cleft palate The Wassermann reaction was negative in all Complete blood studies were entirely normal except for a slight deviation from normal in the differential count These fathers were Rh positive, with 1 exception

From the evidence at hand, and since sterility is not a factor, it must be concluded that the male is not directly responsible Artificial insemination or remarriage may shed light on the subject, except that we have had 4 women with previous erythroblastosis bring forth 4 healthy infants without changing their mates

ANTEPARTUM AND INTRAPARTUM TREATMENT

Intrauterine diagnosis of erythroblastosis is important so that proper therapy can be instituted in order to prevent the condition

marked diminution of congenital syphilis following antiluetic therapy is an example of what can be accomplished by specific antepartum medication It is hoped that specific therapy will be discovered for erythroblastosis We have employed in turn a high protein, high vitamin diet, iodine, and iron, vitamin B₁, Brewer's yeast, calcium and injections of liver, vitamin B complex, 'coppern A' and calcium, without affecting the outcome Bonney and Morton used potassium chlorate, calcium, and wheat germ antenatally, but the infant had erythroblastosis From this evidence, it appears that a well balanced dietary regimen does not prevent the development of the disease in the unborn child

The evaluation of any antepartum therapy is difficult since we have had 4 mothers give birth to normal infants following a previous child with erythroblastosis without special treatment We have treated 3 mothers with frequent injections of synthetic vitamin K (thyloquinone) during the antenatal period, they having had previous infants with erythroblastosis, and each delivered a child with the icterus type of the disease, one of which died

Antepartum transfusions have been considered on the basis that if they are of benefit to the child after delivery, they may be of value before delivery We have had no experience with this procedure

The induction of premature labor has been advocated by Diamond in order to remove the child from its pernicious environment, and also so that transfusions can be given promptly We do not agree with this procedure because there is no adequate method for inducing labor without added risk to the infant Furthermore, prematurity in an infant with erythroblastosis is undesirable, for the hydrops infants are often a month or more before term, and they have a mortality rate of 100 per cent, while the icterus gravis infants are at or near term and have a lower rate of 54 per cent

Dystocia during the delivery may occur due to the ascites or to difficulty with the shoulders especially when the infant is unduly large Delivery in Case 4 resulted in a broad ligament laceration because of shoulder dystocia

Infants delivered by cesarean section have been reported in the literature by Bonney and Morton, A. F. Abt, and Pallos with the delivery of hydropic or icteric infants. This procedure is condemned except when maternal indications justify it, and should never be performed in order to improve the chances for the baby because of the high fetal mortality. We performed the operation on two occasions each time for a definite maternal indication.

Asphyxia within the uterus and asphyxia neonatorum were frequent and resuscitative measures immediately after delivery were often necessary. Therefore the use of analgesia and anesthesia during labor and for delivery should be avoided. If necessary an epizotomy can be performed, local infiltration with novocain being used. The dyspnea and cyanosis seen after delivery is further evidence of faulty oxygenation due to anemia, hydrothorax and ascites.

Therapeutic abortion was never performed in mothers with previous erythroblastotic infants, on that indication alone. However it was a contributing factor in Case 5. However with the recurrence at 50 per cent for mothers who developed erythroblastosis in previous pregnancies and nearly 100 per cent when the first born is affected, erythroblastosis should receive attention from this point of view. In certain instances contraception and adoption of a child may be desirable.

Artificial insemination is frowned upon because of the increasing incidence of erythroblastosis once it has appeared and because paternal investigation has revealed no abnormality. Furthermore in Hiltgenberg's case a mother had several normal children by her first husband and after remarriage had babies with icterus gravis. In Smith's case, a man with a normal child by his first wife had children with icterus gravis by a second wife. However artificial insemination with donor and recipient of the same blood group and Rh negative seems to merit investigation.

PATHOGENESIS OF ERYTHROBLASTOSIS

Many investigators, including Parsons, Hawksley and Gittins are of the opinion that hemolysis is the precursor of the erythroblastemia, and that erythroblastosis is of sec-

ondary development. Abt, von Gierke, Sakmensen and Clifford and Hertig regard the erythroblastosis as primary and a persistence of the embryonic type of blood formation. In fact, Abt states that any theory must begin by explaining the hematopoiesis. Josephs doubts that erythroblastosis is primarily a disease of blood formation since the blood returns rapidly to normal in the first 3 weeks of life. The erythroblastemia and erythroblastosis are probably secondary phenomena, since they exist in other conditions such as congenital syphilis, sepsis neonatorum, and even in premature infants as well as in infants without hydrothorax, icterus, anemia, or hemorrhagic diathesis.

It is futile to argue as to whether hematopoiesis and red cell hemolysis are primary or secondary characteristics both are present. Diamond, Blackfan and Baty regard erythroblastosis as a metabolic disturbance of the hematopoietic system. Darrow concludes that an antigen-antibody reaction explains the pathological processes, i.e. the abnormal red cell destruction, the erythropoiesis, and the hepatic injury and dysfunction. She believes that the placenta transmits the agent from the mother to the fetus. Levine and co-workers reverse the mode of transmission and theorize that when an Rh negative mother becomes pregnant by an Rh positive father, isoimmunization of the mother takes place. Hemolysis may then be initiated in the fetus by the passage of anti Rh agglutinins through the placenta. This theory is very attractive and merits much more investigation which is in progress at the present time.

The disease may begin as a dysfunction of the liver. What is the evidence to justify this point of view? The hydrops and icteric infants showed histological evidence of liver impairment as indicated by the varying degrees of hematopoiesis, deposits of intracellular pigment, and actual degeneration and necrosis of the hepatic cells. Too much emphasis cannot be given the latter findings because of postmortem changes. There was also physiological evidence of liver insufficiency since the infants showed hypoproteinemia, hypoprothrombinemia, a high icterus index and a macrocytic anemia. The patent ductus venosus must also be considered. Finally the

anlage defect which has been postulated for the hematopoietic system can be applied to the liver, for when the child recovers, the hematopoietic system is normal, but there is evidence of residual liver damage. The high incidence of congenital anomalies in our cases makes anlage defect very plausible.

What happens? The liver fails to produce an adequate amount of serum proteins and prothrombin. In some instances this is severe enough to result in universal edema. The capillary endothelium becomes impaired and multiple petechiae, ecchymoses, and hemorrhagic diathesis occur. There is no apparent lack of antianemic principle judging from the hyperplastic state of the bone marrow. However, anemia develops probably because of excessive red cell hemolysis, and is probably initiated by the passage of anti-Rh agglutinins from the mother to the fetus. This goes on for a long time before birth as indicated by the large amounts of pigment deposited in the liver and other organs. This may also represent a failure of the diseased liver to metabolize the bilirubin, and the icterus index rises. Hyperbilirubinemia is also found in normal newborn infants either with or without physiological jaundice according to Waugh and his co-workers. Most authorities regard hyperbilirubinemia as of hematogenous and hepatogenous origin. In erythroblastosis both mechanisms form a vicious cycle and the damaged liver cannot care for the increased amounts of bilirubin, and it may pass into the maternal circulation and elevate the icterus index of the mothers as was frequently observed. When the infant is placed on its own resources after the umbilical cord is ligated, the icterus index of the infants with icterus gravis rose from 86 to 100 units and in subsequent days increased even further to 150 to 400 units. Anemia develops either within the uterus or after delivery. The diseased liver evidently cannot store adequate amounts of antianemic principle as Kracke and Garver state that it normally does. The physiological and pathological changes were invariably most marked in the hydrops infants having a fetal mortality of 100 per cent and were much less pronounced in the icterus infants, which probably accounts for the better survival rate in these infants.

The views of the older investigators that maternal nephritis and cirrhosis of the liver caused fetal hydrops again bear scrutiny. The increased incidence of pre-eclampsia and eclampsia with liver changes in the mothers and definite evidence of liver impairment in their infants with erythroblastosis suggests a common etiology for both. Pregnancy is necessary for the development of toxemia as well as for erythroblastosis. Parsons, Hawksley and Gittins, and de Lange and Arntzenius believe that a toxic agent is responsible for both conditions. Is it possible that the anti-Rh agglutinin of Levine, Katzin, and Burnham is the agent initiating erythroblastosis and toxemia of pregnancy?

CONCLUSIONS

- 1 A classification of erythroblastosis dividing the cases into hydrops, icterus, anemia, hemorrhagic diathesis, and *unclassified* types is presented.
- 2 The total incidence of erythroblastosis was 1/438. The total fetal mortality caused by the disease was 3/2 per cent.
- 3 Multiparity was an associated factor in 92 per cent of the mothers.
- 4 A high incidence of pre-eclamptic type of toxemia was found in the mothers of hydrops cases, and to a less extent in the icterus cases.
- 5 The excessive uterine enlargement, out of proportion to the duration of pregnancy, was shown to be due to the combined weight of the infant and placenta, and not to the "hydramnios."
- 6 The hydrops infants were born a month or more prematurely, whereas the icterus infants were nearer term.
- 7 Asphyxia, either within the uterus or after birth, or during the neonatal life, was a prominent symptom in the fetus. For this reason, if erythroblastosis is suspected before delivery, all analgesia and anesthesia is indicated. Local infiltration can be used for an episiotomy.
- 8 The incidence of postpartum hemorrhage was increased, particularly in the hydrops group.
- 9 The incidence of operative delivery was 56 per cent, the chief indication was fetal distress.

Infants delivered by cesarean section have been reported in the literature by Bonney and Morton A. F. Abt, and Pallos with the delivery of hydrotic or icteric infants. This procedure is condemned except when maternal indications justify it, and should never be performed in order to improve the chances for the baby because of the high fetal mortality. We performed the operation on two occasions, each time for a definite maternal indication.

Asphyxia within the uterus and asphyxia neonatorum were frequent and resuscitative measures immediately after delivery were often necessary. Therefore the use of analgesia and anesthesia during labor and for delivery should be avoided. If necessary an episiotomy can be performed, local infiltration with novocain being used. The dyspnea and cyanosis seen after delivery is further evidence of faulty oxygenation due to anemia, hydrothorax, and ascites.

Therapeutic abortion was never performed in mothers with previous erythroblastotic infants, on that indication alone. However it was a contributing factor in Case 3. However with the recurrence at 50 per cent for mothers who developed erythroblastosis in previous pregnancies and nearly 100 per cent when the first born is affected erythroblastosis should receive attention from this point of view. In certain instances, contraception and adoption of a child may be desirable.

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ondary development. Abt, von Guericke, Salomonson and Clifford and Hertig regard the erythroblastosis as primary and a persistence of the embryonic type of blood formation. In fact Abt states that any theory must begin by explaining the hematopoiesis. Josephs doubts that erythroblastosis is primarily a disease of blood formation, since the blood returns rapidly to normal in the first 3 weeks of life. The erythroblastemia and erythroblastosis are probably secondary phenomena, since they exist in other conditions such as congenital syphilis, sepsis neonatorum, and even in premature infants, as well as in infants without hydrops, icterus, anemia, or hemorrhagic diathesis.

It is futile to argue as to whether hematopoiesis and red cell hemolysis are primary or secondary characteristics both are present. Diamond, Blackfan and Baty regard erythroblastosis as a metabolic disturbance of the hematopoietic system. Darrow concludes that an antigen-antibody reaction explains the pathological processes, i.e. the abnormal red cell destruction, the erythropoiesis and the hepatic injury and dysfunction. She believes that the placenta transmits the agent from the mother to the fetus. Levine and co-workers reverse the mode of transmission and theorize that when an Rh negative mother becomes pregnant by an Rh positive father isoimmunization of the mother takes place. Hemolysis may then be initiated in the fetus by the passage of anti Rh agglutinins through the placenta. This theory is very attractive and merits much more investigation which is in progress at the present time.

The disease may begin as a dysfunction of the liver. What is the evidence to justify this point of view? The hydrops and icterus infants showed histological evidence of liver impairment as indicated by the varying degrees of hematopoiesis, deposits of intracellular pigment, and actual degeneration and necrosis of the hepatic cells. Too much emphasis cannot be given the latter findings because of postmortem changes. There was also physiological evidence of liver insufficiency since the infants showed hypoproteinemia, hypoprothrombinemia, a high icterus index, and a macrocytic anemia. The patent ductus venosus must also be considered. Finally the

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anlage defect which has been postulated for the hematopoietic system can be applied to the liver, for when the child recovers, the hematopoietic system is normal, but there is evidence of residual liver damage. The high incidence of congenital anomalies in our cases makes anlage defect very plausible.

What happens? The liver fails to produce an adequate amount of serum proteins and prothrombin. In some instances this is severe enough to result in universal edema. The capillary endothelium becomes impaired and multiple petechiae, ecchymoses, and hemorrhagic diathesis occur. There is no apparent lack of antianemic principle judging from the hyperplastic state of the bone marrow. However, anemia develops probably because of excessive red cell hemolysis, and is probably initiated by the passage of anti-Rh agglutinins from the mother to the fetus. This goes on for a long time before birth as indicated by the large amounts of pigment deposited in the liver and other organs. This may also represent a failure of the diseased liver to metabolize the bilirubin, and the icterus index rises. Hyperbilirubinemia is also found in normal newborn infants either with or without physiological jaundice according to Waugh and his co-workers. Most authorities regard hyperbilirubinemia as of hematogenous and hepatogenous origin. In erythroblastosis both mechanisms form a vicious cycle and the damaged liver cannot care for the increased amounts of bilirubin, and it may pass into the maternal circulation and elevate the icterus index of the mothers as was frequently observed. When the infant is placed on its own resources after the umbilical cord is ligated, the icterus index of the infants with icterus gravis rose from 86 to 100 units and in subsequent days increased even further to 150 to 400 units. Anemia develops either within the uterus or after delivery. The diseased liver evidently cannot store adequate amounts of antianemia principle as Kracke and Garver state that it normally does. The physiological and pathological changes were invariably most marked in the hydrops infants having a fetal mortality of 100 per cent and were much less pronounced in the icterus infants, which probably accounts for the better survival rate in these infants.

The views of the older investigators that maternal nephritis and cirrhosis of the liver caused fetal hydrops again bear scrutiny. The increased incidence of pre-eclampsia and eclampsia with liver changes in the mothers and definite evidence of liver impairment in their infants with erythroblastosis suggests a common etiology for both. Pregnancy is necessary for the development of toxemia as well as for erythroblastosis. Parsons, Hawksley and Gittins, and de Lange and Arntzenius believe that a toxic agent is responsible for both conditions. Is it possible that the anti-Rh agglutinin of Levine, Katzin, and Burnham is the agent initiating erythroblastosis and toxemia of pregnancy?

CONCLUSIONS

- 1 A classification of erythroblastosis dividing the cases into hydrops, icterus, anemia, hemorrhagic diathesis, and *unclassified* types is presented.
- 2 The total incidence of erythroblastosis was 1.438. The total fetal mortality caused by the disease was 3.2 per cent.
- 3 Multiparity was an associated factor in 92 per cent of the mothers.
- 4 A high incidence of pre-eclamptic type of toxemia was found in the mothers of hydrops cases, and to a less extent in the icterus cases.
- 5 The excessive uterine enlargement, out of proportion to the duration of pregnancy, was shown to be due to the combined weight of the infant and placenta, and not to the "hydramnios."
- 6 The hydrops infants were born a month or more prematurely, whereas the icterus infants were nearer term.
- 7 Asphyxia, either within the uterus or after birth, or during the neonatal life, was a prominent symptom in the fetus. For this reason, if erythroblastosis is suspected before delivery, all analgesia and anesthesia is indicated. Local infiltration can be used for an episiotomy.
- 8 The incidence of postpartum hemorrhage was increased, particularly in the hydrops group.
- 9 The incidence of operative delivery was 56 per cent, the chief indication was fetal distress.

10. When the fetus is macerated histological examination of the placenta and of the liver by means of special pigment stains offers a good opportunity for diagnosis.

11. The obstetrical history of the patient should replace the "family history" since the disease is not familial in the strict sense.

12. The degree of parity is important in predicting a subsequent case of erythroblastosis. The incidence of erythroblastosis in pregnancies after its initial appearance is approximately 50 per cent. If the first born had the disease the incidence for subsequent infants is nearer 100 per cent.

13. Case histories of hydrops and eclampsia identical twins with erythroblastosis, erythroblastosis with hemorrhagic diathesis as the initial symptom, hydrops with survival for 11 days icterus gravis diagnosed *intra uterine* and hydrops fetalis diagnosed *intra uterine* were presented.

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19. The immediate treatment of erythroblastosis is to combat asphyxia. Repeated transfusions from a compatible donor in order to provide protein, prothrombin and blood cells for the infant, are imperative.

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10. When the fetus is macerated histological examination of the placenta and of the liver by means of special pigment stains offers a good opportunity for diagnosis.

11. The obstetrical history of the patient should replace the "family history" since the disease is not familial in the strict sense.

12. The degree of parity is important in predicting a subsequent case of erythroblastosis. The incidence of erythroblastosis in pregnancies after its initial appearance is approximately 50 per cent. If the first born had the disease, the incidence for subsequent infants is nearer 100 per cent.

13. Case histories of hydrops and eclampsia. Identical twins with erythroblastosis, erythroblastosis with hemorrhagic diathesis as the initial symptom, hydrops with survival for 11 days, icterus gravis diagnosed *intra uterine* and hydrops fetalis diagnosed *intra uterine* were presented.

14. Maternal blood studies were usually normal save for an increased icterus index and uric acid probably due to maternal liver damage accompanying toxemia. The serum proteins were generally reduced. Several of the mothers were Rh negative.

15. The infants had a high incidence of congenital anomalies.

16. Autopsy often revealed some degree of liver degeneration, pigment deposits and hematopoiesis, which were usually most marked in hydrops cases.

17. Complete studies of cord blood are presented. The number of erythroblasts and normoblasts, as well as their ratio are important diagnostic criteria.

18. The serum proteins and the prothrombin concentration of cord blood were reduced especially in the hydrops cases while the icterus index was greatly increased, also to a greater extent in the hydrops group. These changes together with the macrocytic anemia are interpreted as physiological evidence of impaired liver function.

19. The immediate treatment of erythroblastosis is to combat asphyxia. Repeated transfusions from a compatible donor in order to provide protein, prothrombin and blood cells for the infant, are imperative.

20. The mortality for the hydrops cases was 100 per cent, for the icterus group 54 per cent.

21. Correct antepartum diagnosis was made in 8 of 10 attempts and the important criteria were stated.

22. The Buddha-like habitus of the fetus *in utero* by x ray examination is an important diagnostic feature.

23. Paternal studies including blood and semen failed to disclose any abnormality. Several fathers were Rh positive except in one instance.

24. The management of a patient with suspected erythroblastosis is given. Cesarean section should not be performed except for maternal indication.

25. The probable pathogenesis of erythroblastosis is presented on the basis of liver dysfunction. Anatomical and physiological evidence is given to support this view. The significance of the Rh factor was mentioned.

26. Erythroblastosis runs part of its course *in utero* and the obstetrician and pediatrician in consultation are in a strategic position for antepartum diagnosis.

27. Hematological studies of the cord blood afford a prompt and simple method of making the diagnosis at the time of the delivery so that treatment may be instituted promptly.

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TREATMENT OF FRESH TRAUMATIC AND CONTAMINATED SURGICAL WOUNDS

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IN the evaluation of a method of management of fresh contaminated wounds three questions must be answered. Does the method render the wound aseptic? If not, does the method injure the tissues and thereby interfere with the normal mechanism of defense against infection and of repair? And third, the all important one. What are the clinical results of the method? In the report which follows an attempt is made to answer these questions.

We believe that there is ample experimental and clinical evidence that no method in use today renders a contaminated wound absolutely free of bacteria. As a matter of fact, surgical asepsis is never absolute and even in so called sterile operative surgery the sterility is always relative. Therefore the question as to whether a given wound remains aseptic or becomes infected and suppurates depends upon two factors the quantity and the character of the micro-organisms which remain in the tissues and the effectiveness of the defense mechanism.

We also believe that there is ample experimental and clinical evidence that the chemical bactericidal agents, which are so generally used to disinfect wounds, destroy or devitalize the tissue cells with which they come in contact and thereby seriously impede the inflammatory response and impair the effectiveness of the natural mechanism of defense.

If the bactericidal agents always rendered wounds free from bacteria, the injury inflicted upon the tissues would be of little consequence. However failing to destroy all the micro-organisms, they leave the tissues damaged and less capable of coping with the bacteria which remain viable.

Both from experimental and clinical evidence accumulated by us and from similar data reported by others, we believe that wounds can be rendered as relatively sterile by me-

chanical washing with very copious irrigations of isotonic salt solution as by the application of bactericidal agents. This method has the very important advantage that it leaves the tissues essentially uninjured to mobilize the natural defenses to deal with the microorganisms which remain.

An abundance of evidence has accumulated to establish the sulfonamides as very effective bacteriostatic agents for certain bacteria. From the experimental data reported by others and from that which follows it is apparent that sulfanilamide applied directly to the tissues causes no apparent damage to the cells and does not alter the normal course of repair of either bone or soft tissues. Actually in our animals it facilitated repair in contaminated wounds by preventing infection.

EXPERIMENTAL OBSERVATIONS

I Tissue response to application of sulfanilamide normal salt solution and a few of the antiseptic or bactericidal preparations most commonly employed. In each of 4 rabbits 5 small transverse incisions were made into the subcutaneous tissue of the abdominal wall on each side of the midline at regularly spaced intervals. Rigidly aseptic technique was employed. One wound served as a control. One was washed vigorously with isotonic salt solution. The 8 remaining were painted thoroughly with one of the 8 agents: tincture of green soap, ether alcohol tincture of iodine sulfanilamide powder and solutions I, II and III. The unnamed solutions are the commercial preparations most widely used in the United States. The wounds were closed with adhesive tape and covered with sterile dressings.

In a second series of 8 rabbits approximately 5 minims of each of the 9 test agents was injected into the subcutaneous tissues of the abdominal wall with hypodermic needles. Points of injection were marked with India ink.

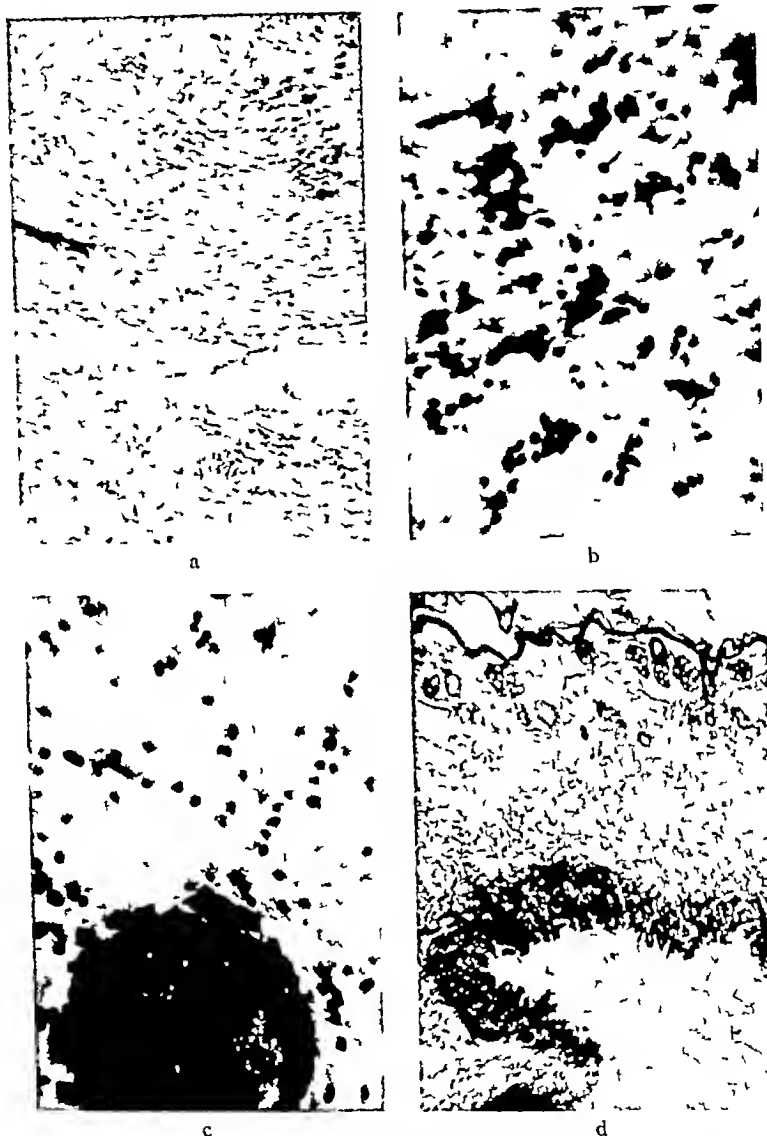


Fig 1 a, Mild inflammatory response 12 hours after 5 minims of ether had been injected into the tissues. Note slight edema and leukocytic infiltration. b, A high power magnification of a shows swollen tissue cells with poorly staining nuclei. c, Moderate inflammatory reaction 4 hours after injection of alcohol. Note moderate edema, round cell infiltration, pale staining tissue cells and a thrombosed blood vessel. d, Gross tissue necrosis and severe inflammatory response (abscess) at the site of injection of 5 minims of the tincture of green soap. Injection made 12 hours previously.

One animal in the first series and 2 in the second were sacrificed at each of four intervals following incision or inoculation, 4, 12, and 48 hours and 5 days. Blocks of skin and subcutaneous tissue containing the sites of incision

or inoculation were excised and studied microscopically. Normal salt solution provoked essentially no more tissue damage or inflammatory response than did mere trauma as measured by the controls.

Similarly there was no evidence that sulfanilamide injured tissue cells or that it incited more than a feeble inflammatory response. All of the other agents consistently gave rise in various degree to tissue reaction to injury. Curiously either was the least, and green soap the worst offender. The latter produced gross tissue necrosis with abscess formation in more than half of the specimens. Antiseptics II and III also were provocative of gross necrosis and abscess formation. Although iodine and alcohol caused moderate to marked inflammatory reactions no gross evidence of necrosis was found in the specimens.

Photomicrographs of specimens illustrating degrees of tissue reaction appear in Figure 1.

II Contaminated compound fractures. In 18 rabbits segments of both radial shafts measuring approximately 0.5 centimeter were removed subperiosteally and filled with constant broth suspensions of hemolytic streptococci, hemolytic colon bacilli and Staphylococci albi. The latter two cultures were obtained originally from infected wounds of rabbits.

Four animals were used as controls and after inoculation the wounds were closed without further treatment. Two of these animals died within a few days; the 2 others developed abscesses at the operative sites in both legs which drained for many days. Only 1 of the 4 fractures developed union and this was rather meager. In 3 fractures segments of the shaft had obviously been sequestered. In the 14 remaining animals the wounds were inoculated with the cultures, closed for 10 minutes, and then re-opened and filled with the test agents and antiseptic solutions used in experiment I. Thus 2 rabbits were utilized for each antiseptic agent.

A brief summary of the results in these 14 animals follows, and illustrative roentgenograms appear in Figure 2.

Wounds lavaged with salt solution and filled with sulfanilamide powder: 4 wounds—no infection and all healed by primary intention; 4 fractures—all healed normally; 1 bony union.

Sulfanilamide only: 4 wounds—1 healed by primary intention, mildly and grossly infected; 4 fractures—in all, bone repaired normally.

3 Fiber: 4 wounds—1 infected, grossly; 4 fractures—1 failed to unite and partially repaired.

4. Alcohol: 4 wounds—1 grossly infected (one in each rabbit); 4 fractures—both failed to repair; 1 rabbit died after 5 days—no gross findings of consolidation.

5. Tincture of iodine: 4 wounds—2 grossly infected and superficially infected; 4 fractures—1 totally ununited and partially repaired.

6. Antiseptic I: 4 wounds—1 grossly infected (one in each animal); 4 fractures, one totally ununited and one partially repaired; 1 rabbit died after 3 days, no definite cause of death demonstrable.

7. Antiseptic III: 4 wounds—3 grossly and superficially infected; 4 fractures—4 non-unions.

8. Tincture of green soap: 4 wounds—all grossly infected; 4 fractures—both failed to repair. One rabbit died after 1 day from diarrhea and inanition.

III Influence of the topical application of sulfanilamide upon the repair of bone and soft tissues. In 12 rabbits the radius of each leg was exposed and fractured by a transverse saw-cut. The wound of each left leg was closed to serve as a control; that of each right leg filled with powdered sulfanilamide and closed tightly. Two rabbits died and there were 1 grossly infected wounds of the control legs.

The animals were killed and the specimens recovered for x-ray and microscopic study 2, 3, 4, 5 and 6 weeks after operation.

There was no gross or microscopic evidence of any difference in the rate or character of the repair of either the soft tissues or the bone in the control as opposed to the sulfanilamidized wounds. A comparison of the progress of bone repair is shown in Figure 3.

EXPERIMENTAL RESULTS

From these studies certain deductions can be made and although these deductions alone are not necessarily clinically applicable they would seem to become so when supported by similar if not identical, clinical observations.

It is apparent that the commonly used bactericidal or antiseptic solutions did not render all wounds completely free from bacteria and furthermore that these agents caused injury to the tissues varying from edema with minor cell death to gross necrosis of the tissues. It is also apparent that these solutions caused interference with the repair of bone presumably the result of devitalization of the osteogenic elements. It is noteworthy that other



Fig 2 Fractures of the radius induced by resections of 0.5 centimeter segments of the shafts. Wounds inoculated with cultures of hemolytic streptococcus and colon bacillus and *Staphylococcus aureus*. Roentgenograms at 6 weeks. From left to right 1, Control—Wound grossly infected, an associated osteomyelitis with sequestration followed by union with a thin bridge of new bone. 2, Tincture of green soap—Suppuration, no new bone, non union. 3, Antiseptic I—as in 2. 4, Iodine—as in 2 except proliferation of new bone. 5, Alcohol—suppuration but proliferation of new bone with some union of fragments. 6, Saline irrigation and sulfanilamide—no infection and good bony union.

caused relatively little injury to tissues and tincture of green soap severe tissue damage.

Although sulfanilamide caused some edema response in the tissues it was relatively innocuous and there was no evidence that it altered the normal course of repair of either soft tissue or bone. Key and Burford likewise found no evidence of retardation of healing of uninfected fractures and soft tissue wounds in animals as a result of local implantation of sulfanilamide.

Sulfanilamide was very effective, but not completely so, in preventing infection in wounds grossly contaminated with specifically pathogenic micro-organisms. These observations confirm those of Jensen et al., and of Key and Burford. The latter found sulfanilamide more effective than the other sulfonamides.

In the animals in which the contaminated wounds were thoroughly washed with salt solution before sulfanilamide powder was applied, infection was entirely eliminated. It is our impression that the thorough washing of the wounds with salt solution disposed of most of the bacteria and was the more important step, while sulfanilamide, as a bacteriostatic agent, contributed an additional safeguard. Furthermore, there was no evidence that either agent used singly or both used jointly caused any damage to tissues.

CLINICAL OBSERVATIONS

Irrespective of the results obtained from animal investigation the merits of a method of

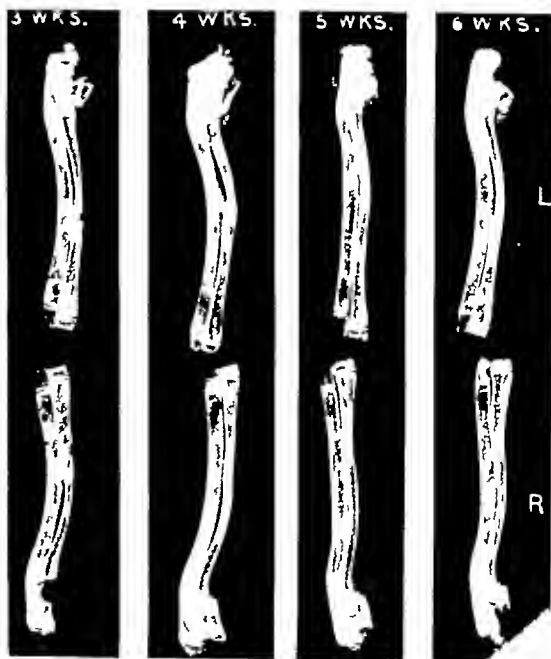


Fig 3 In these animals the topical application of sulfanilamide powder (lower row) did not alter the rate and completeness of fracture repair as compared to controls (upper row).

treatment can be determined with finality only through clinical application. Therefore, in the way of final judgment a brief report of the results obtained in 25 consecutive cases with major fresh wounds follows.

In 20 of the 25 cases there was good evidence from history or by fact that soiling of the wounds had occurred either by penetration of a foreign body or by exteriorization of bone. All of these patients were treated by us within 8 hours of the time of injury and in general all received the same type of treatment. It consisted of

- 1 *Rapid preliminary treatment of shock* in all cases so afflicted. Plasma being unavailable, blood transfusions were used freely for this purpose.

- 2 After alleviation of shock an *evaluation of extent of injury* was made, including roentgenograms and detailed examinations for evidence of loss of function of individual tendons and nerves.

- 3 *Cleansing and débridement* In the compound fractures in which one of the fragments protruded through a laceration of the skin, no attempt was made to replace this fragment until it had been thoroughly cleansed. We believe that this principle should be followed whenever facilities for thorough cleansing are immediately available. A fragment which has been exteriorized is always soiled and the soft tissue bed from whence it emerged is often either totally or relatively sterile. Therefore cleansing the fragment before replacing it accomplishes the major act in preventing infection and also avoids contamination of the soft tissues. Before the exteriorized fragment was cleansed the skin for a wide area about the wound was rendered surgically clean by scrubbing it with a sterile hand brush for 3 or 4 minutes with a stream of sterile water and green soap constantly flowing over the area. The bone was then washed by gentle brushing of all surfaces with a new sterile brush, while normal salt solution (and only salt solution) was constantly poured over it. Solutions other than saline such as soap and antiseptics were used only in preparing the skin.

In those cases in which the soiled fragment had been replaced before the patient came into our hands, we exteriorized this fragment after

the skin had been cleansed and washed as described.

In either case before the fragment was replaced all parts of the wound were irrigated with large quantities of normal salt solution. It must be emphasized at this time as it will be repeatedly that these irrigations must be copious, many liters of saline being used. The wound should be retracted as necessary to expose its entire extent and all surfaces should be gently agitated with gauze while the solution is flowing over them.

The fragment was then replaced and all torn and devitalized bits of fat, muscle and fascia were excised. Because crushed skin does not heal readily and often separates the crushed and devitalized margins of the skin flaps were excised whenever feasible. The wound was then again copiously irrigated with normal salt solution, its surfaces covered with a thin layer of sulfanilamide powder and the skin closed usually without drainage.

The fractures were reduced through the open wound in some instances and after skin closure in others. It is our opinion that if these fractures have been thoroughly cleansed and prepared as here outlined they may be handled essentially as clean simple fractures. This applies to the use of metallic and other foreign material for internal fixation. Whenever indicated we have made use of internal fixation and have had no occasion to regret it.

The technique of cleansing compound fracture wounds in which there was no protruding fragment, and of all other types of wounds, differed only in respect to one important detail. This the initial step, consisted of closing the wound temporarily with Michel clips to prevent soiling it while the skin was being prepared. This not only prevented the dirty wash water from running into the wound but also permitted scrubbing across the approximated skin edges. After the skin had been rendered surgically clean the clips were removed and the wound was opened widely and irrigated and débrided. If the laceration of the skin was too small to permit adequate exposure for purposes of inspection, débridement, and irrigation, it was enlarged. Regardless of the degree of soiling severed tendons and nerves in wounds treated within 8 hours of the time of

injury were sutured immediately. This can be done with little risk of infection if the wound has been properly prepared by copious irrigations and thorough débridement and by the topical application of sulfanilamide.

4 *Prophylaxis* Tetanus antitoxin was administered routinely. Clostridium welchii and perfringens antitoxin was not used.

Routinely we gave all wounds immediately a course of x-ray therapy upon the assumption that these rays are as effective in preventing infection from Clostridium welchii and other gas forming anaerobes as they are in the treatment of established infections.

5 *All wounds of the extremities were immobilized* either in traction or by splinting or casting. If a cast had been applied a small window was immediately made to expose the wound for purposes of frequent direct inspection and palpation.

6 *All patients with major wounds were hospitalized* for at least 48 hours. During this period they were kept at complete bed rest with the injured part, if an extremity, elevated above heart level. This period of hospitalization was insisted upon to assure constant observation by trained observers. During this period a minimal fluid intake of 2,500 cubic centimeters was maintained by mouth or parenterally when the oral route was not available or adequate. Blood was given until relatively normal levels of hemoglobin and red cells had been attained. Vitamin B-complex and Vitamin C were given in therapeutic doses routinely.

This series consisted of 25 cases, 14 cases with compound fractures of the major long bones, 9 with major lacerations, and 2 with shotgun wounds received at close range. Not one patient in the entire group developed a primary infection or a subcutaneous suppurative process and in 13, or 50 per cent of the cases, the wounds healed *per primam*. Both shotgun wounds, one of the thigh and one of the flank, were left open because it was impossible to close them after the shredded wound margins had been excised. In 8 of the 14 cases with compound fractures, and in 2 of the 9 with major lacerations, there was failure of primary healing of portions of the approximated skin edges. This we attributed to tension and to devitalization of the edges of the

skin flaps as the result of the original trauma. In all but one of these cases retraction of the flaps left only superficial open surfaces which healed by granulation. One compound fracture of the tibia re-compounded when the skin flaps retracted. In only 1 case was the granulating surfaces sufficiently large to make the grafting of skin a feasible aid to more rapid epithelization. All fractures promptly united and in no case did osteomyelitis develop.

In allocating credit for the prevention of infection in these cases it is our impression that, as in the case of the experimental animals, the implanted sulfanilamide powder played a large part, but a part secondary to the thorough débridement and the profuse mechanical washing with saline. That sulfanilamide is a valuable adjunct is attested to by the reported clinical experiences of many observers among whom may be mentioned Jensen et al, Stuck et al, Key and Lembeck, Campbell and Smith, Hodgeson and McKee, Johnson and Davis, Colebrook, and Brown et al.

Although there is good evidence that it is safe to place unsterilized sulfanilamide powder in wounds we have used only sterilized powder. By a very simple method the powder can be sterilized in an autoclave and at the same time be kept dry. The powder is placed in a glass container with a narrow neck and around its mouth two sheets of waxed paper are tightly secured. Prepared in this way the powder remains unchanged and as such retains its adhesive quality for the tissues.

WAR WOUNDS

Logically, the principles of treatment outlined should be effective in fresh injuries inflicted in military combat. The application of these principles under circumstances of war presents obvious difficulties. The foremost difficulty would be the provision of an adequate supply of sterile normal salt solution for copious irrigation of wounds. It is probable that this need could be met even near the line of battle by means of large tanker trucks from which the solution could be piped directly to dressing stations. It is also probable that such tankers could be provided with means for sterilizing and replenishing the supply as used

The entire extrahepatic biliary system has a dual nerve supply parasympathetic fibers from the vagus nerve and sympathetic fibers from the splanchnic nerves. A controversy which still remains unsettled, concerns which of the two carry motor and which inhibitory impulses. More recent work suggests that motor and inhibitory fibers may be found in the same nerve (23).

This discussion of the nervous supply of the extrahepatic biliary tract has considerable practical import, for from it evolved several therapeutic and diagnostic developments. Foster in 1880, was the first to suggest a reciprocal innervation between gall bladder and sphincter of Oddi i.e., when the gall bladder contracted, the sphincter relaxed. The reader is referred to the bibliography of Ivy for the extensive literature on this particular phase of the subject.

The maximal intragall-bladder pressure does not exceed the secretory pressure of the liver thereby permitting a free flow of hepatic bile into the gall bladder which occurs during the fasting period, when the sphincter is closed. With the first meal containing a stimulus for gall-bladder contraction the sphincter relaxes and the intraductal pressure falls to a level against which the gall bladder can now easily contract and evacuate itself (9, 27) either by reflex or by the same factor which makes the sphincter open itself. The normal physiological stimulus for the evacuation of the gall bladder is the passage of gastric chyme, following ingestion of fat or protein, into the duodenum.

Whether the sphincteric action of the end of the common duct is due to a true and independent sphincter or is determined by duodenal activity alone, or is regulated by both, has provoked much debate. A great part of the difficulty can be ascribed to the problems inherent in attempting to separate the activity of two so closely approximated structures. That duodenal peristalsis plays a rôle in the flow of bile into the duodenum is a fact accepted by the majority of workers. However many have found that bile sometimes may be discharged without regard to duodenal activity. We believe our method has clarified this situation in a graphic manner.

That the flow of bile is dependent upon changes in intra-abdominal pressure incident to respiration has been thoroughly disproved (8, 15, 17) despite the insistence of some (4, 7, 20, 35).

That a discussion of the physiology of the mechanism of bile flow bears considerable practical import can be illustrated best by the development in recent years of a relatively large literature on biliary dyskinesia or "dysmynergia." Interest in this subject was aroused when surgeons could not account for the obstruction to the biliary tract with the usual pathological findings. A physiological obstruction of the sphincter of Oddi was then proposed as a possible etiological factor. The reader is referred to extensive reviews of this interesting subject (2, 17, 29).

METHODS

The method in most common use today for determining the pressure within the common bile duct goes back to Oddi in 1837. He severed the common bile duct and inserted a cannula into it, directed toward the duodenum. The cannula was attached to a mercury column and the level of the column at which drops of mercury were seen to appear at the papilla of Vater was taken as the intraductal pressure. Oddi found it to be the equivalent of 675 millimeters of water. Archibald used this method in attempting to show that bile pancreatitis must be due to a spasm of the sphincter of Oddi, but was the first to use a water manometer. He found intraductal pressures of 180 to 330 millimeters of water which rose to 800 millimeters on application of 3 per cent hydrochloric acid directly to the papilla. Mann (26) using this technique has studied the sphincteric resistance in a great variety of species. Other methods of studying the sphincteric mechanism which have been used include visual observations of the exposed papilla of anesthetized animals, comparing the effects before and after section or cannulization, transplanting the proximal part of the choledochus above the ampulla, creating external duodenal biliary fistulas, and measuring the height at which a column of fluid ceases to perfuse through the common duct. Loeth (23) in Ivy's laboratory perfected a cannula

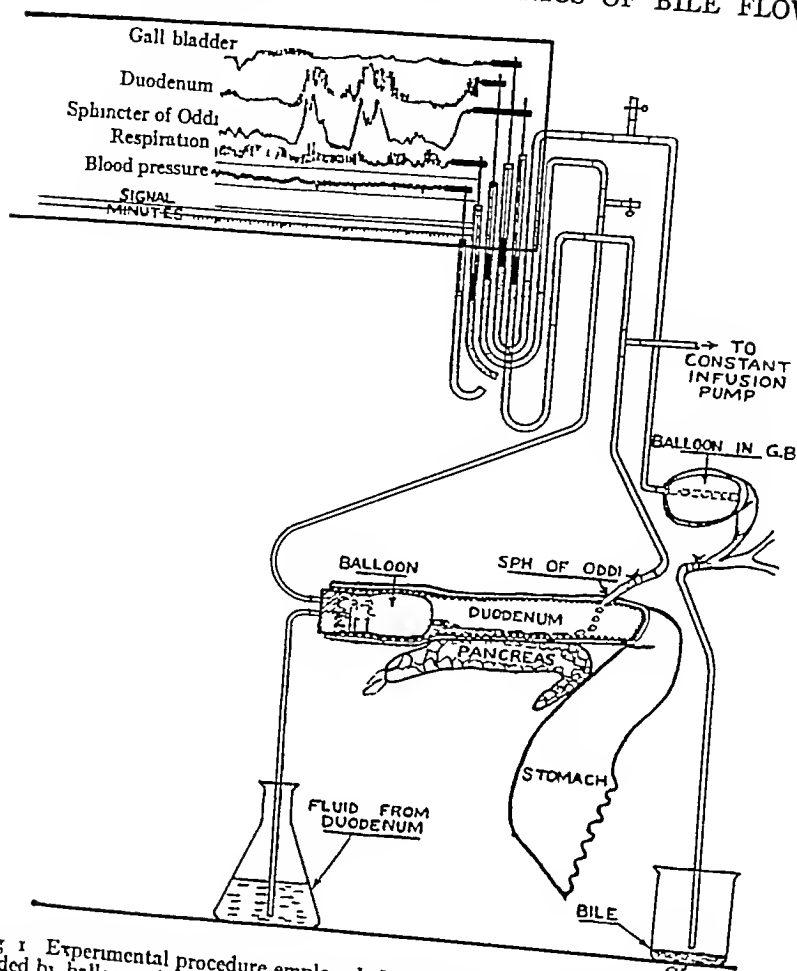


Fig 1 Experimental procedure employed Motility of gall bladder and duodenum recorded by balloon-oil manometer systems Resistance of sphincter of Oddi to a constant perfusion with 0.9 per cent saline recorded by another oil manometer Respiration recorded by balloon placed between the liver and diaphragm, leading to a fourth oil manometer Blood pressure recorded by mercury manometer Glass cannula projecting beyond duodenal balloon for drainage of perfusion fluid entering through the sphincter of Oddi and for injecting solutions into the duodenum

with which the gradient of pressure within the common bile was determined He also recorded simultaneously duodenal activity and the rate of drop perfusion through the sphincter Konan, in Japan, used a technique similar to ours, but in his experiments, the rate of perfusion through the sphincter of Oddi does not seem to have been constant, his results were not recorded together, and he did not publish any of his records

Our own experimental procedure is illustrated in the accompanying diagram (Fig 1) Fourteen experiments were completed on nor-

mal healthy fasting dogs under light pentobarbital (nembutal) anesthesia (25 mgm per kgm body weight, intravenously) In 3 dogs supplementary ether anesthesia was required for maintenance, all of these 3 were female dogs External heat was applied and parental solutions were administered, if necessary

Condom balloons were inserted into the gall bladder and lowermost portion of the duodenum The cystic duct was not ligated, to prevent vascular changes within the gall bladder, and in order not to destroy reflex

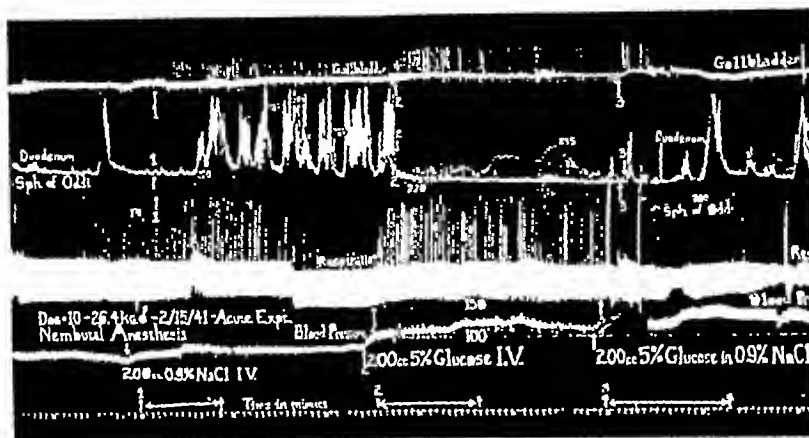


Fig 3 At 1, normal saline, given intravenously, produced 50 to 100 millimeter rises in sphincteric pressure with simultaneous increase in duodenal tone and motility. At 2, 5 per cent glucose, intravenous, produced a marked depression of duodenal motility and tonus with a gradual rise in sphincteric resistance. At 3, a combination of glucose and saline, intravenous, produced similar rises in sphincteric pressure as when saline alone was given, but the duodenal response was less than with saline alone. Gall bladder tone and motility increased.

RESULTS

Normal activity The sphincter of Oddi has a regular and distinct tonus rhythm. There are 10 to 20 millimeter changes in pressure which are manifested as rather large and irregular fluctuations on a control tracing. Superimposed upon these large fluctuations are 2 to 3 millimeter oscillations. We have not been able to discern three separate types of motility as described by Higgins and Mann. The sphincter tonus is completely independent of the tonus of the gall bladder, and there is a surprising lack of correlation between duodenal and sphincter activity. We have frequently noted subtetanic contractions of the duodenum to occur during normal control periods which were not associated with any significant changes in the intraductal pressures (Fig 2). In some animals it is quite true that marked duodenal spasm was coincident with spasms of the sphincter, but even in these animals this was not invariably the rule.

The motility of the gall bladder is usually manifested as 3 to 5 millimeter changes in tonus occurring at a rhythmic rate, gall-bladder activity under normal conditions was found to be independent of the spontaneous activity of the duodenum or of the sphincter and vice versa. Marked respiratory effort produc-

ing deep excursions of the diaphragm could be immediately recognized in the gall-bladder tracing and were not confused with true alterations in gall-bladder activity. At no time was there a correlation between the state of tone of each of these three organs with blood pressure and respiratory changes.

Responses to physiological intravenous solutions The administration of 200 cubic centimeters of normal saline intravenously was always followed by a significant increase in sphincter tone averaging about 100 millimeters (18 experiments on 12 animals) usually associated with a marked increase in duodenal tone and motility (Fig 3). There was no consistent change in gall-bladder motility due to normal saline and the blood pressure showed a consistent and prolonged elevation during the administration of the solution. The use of hypertonic saline, 10 to 20 cubic centimeters of 20 per cent sodium chloride intravenously, was followed by even more marked results in the direction produced by normal saline (Figs 2 and 4). The gall bladder showed a consistent decrease in tonus in every 1 of the 20 instances in which hypertonic saline was used. These responses were more immediate and more marked than with normal saline, but less prolonged. The observations on the duodenum are in line with pre-

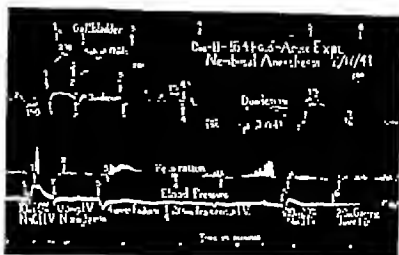


Fig. 4. The effects of drugs on spasm induced by hypertonic intravenous saline. At 2, 0.5 milligram nitroglycerin, intravenous, produced a sharp transitory drop in sphincter pressure with a similar fall in duodenal tone. At 3, 4 units of padutin had similar but more prolonged effect on the sphincter without affecting duodenal activity and in addition, produced gall bladder contraction. At 4, 50 milligrams traseptin produced a prolonged lowering of sphincter resistance 5 minutes after injection, and the following intravenous injections of hypertonic saline at 5, or of gastric juice—intraduodenal—at 6 which usually produced marked sphincter spasm were much less effective following the transient. Duodenal motility was practically abolished by traseptin.

vious work on the effect of normal and hypertonic solutions of saline on intestinal activity (16, 19, 31). The effects of normal saline on sphincter and duodenum were abolished by atropine in one instance and decreased by traseptin A in another. These agents have little influence on the spasm producing effect of hypertonic saline (Fig. 4). Nitroglycerine and padutin¹ produced temporary relaxation of sphincteric spasm induced by hypertonic sodium chloride (Fig. 4).

Intravenous injection of 300 cubic centimeters of 5 per cent dextrose in distilled water was given intravenously to 8 animals. Sphincter resistance increased in 3, was not influenced in 3 and decreased in 2. However in practically every instance there was a marked decrease in duodenal tone and motility. It is interesting to note that a 30 to 50 millimeter increase in sphincteric resistance occurred in spite of the decrease in duodenal activity (Fig. 3).

The intravenous injection of a 5 per cent glucose solution after intraduodenal adminis-

¹Vanadepren was a gift of Knott and Frey.

tration of magnesium sulfate and sodium sulfate was associated with a rise in sphincteric pressure but with a continued depression of duodenal activity. Twenty to 40 cubic centimeters of a hypertonic solution of dextrose was employed in 9 dogs with effects no more marked and less prolonged than with 5 per cent dextrose. Reports are contradictory relative to the effect of intravenous dextrose on intestinal peristalsis, but our results are in agreement with the work of Ochsner et al. (11, 12). The rise in blood pressure seen was frequently greater than with normal saline.

Intravenous injection of 300 cubic centimeters of 5 per cent dextrose in 0.9 per cent saline was employed in 8 dogs with unpredictable results somewhere intermediate between the effects produced by either solution alone. The combination of those two solutions produced greater rises in blood pressure than either alone (Fig. 3).

ANALYSIS OF STUDY

The graphic evidence of the independence in the activity of the sphincter of Oddi and the

duodenum during a control period offers convincing proof in confirmation of the work of many. We have observed similar independent responses to drug stimulation. It must be clearly stated, however, that most frequently these two structures respond in an identical manner, if not at the same interval.

The effects of intravenous injection of normal saline solution on the duodeno-sphincteric mechanism was unexpected and challenging. In most experiments a prolonged and extensive rhythmic wave of contraction or spasm was produced in both the sphincter and duodenum. This is best demonstrated in Figure 1. The gall bladder did not usually react and atropine or traserin abolished or diminished this effect of normal saline solution. This latter observation may be of importance in treatment of stones in common duct when intravenous saline has to be given.

Another physiological solution, namely 5 per cent glucose in distilled water did not affect the duodenum as did saline solution, but produced a moderate but prolonged contraction of the sphincter of Oddi, as demonstrated in Figure 3. The duodenum was relaxed following the injection of glucose.

Therefore a combination of both was tried, namely 5 per cent glucose in 0.9 per cent sodium chloride. This was followed by a slight contraction of the gall bladder, a primary depression of sphincteric and duodenal tone which would have permitted emptying of the gall bladder and which lasted for several minutes following this, waves of contraction of the sphincter and of the duodenum occurred (Fig. 3). If these experiences can be applied to man, and they may be easily tried without harm to the patient, it may be a good procedure in cases of stones impacted in the common duct, and particularly in the ampulla.

Hypertonic solutions of sodium chloride in small amounts, administered intravenously, were consistently followed by great rises of sphincteric tone, as well as of duodenal tone and contractions (Figs. 2 and 4). The gall bladder showed a small and short relaxation. Again, this observation may be of importance if it can be applied to the human. Hypertonic saline has been recommended for treatment of paralytic ileus, but in case of impacted

stone it may be contraindicated because a prolonged spasm of the duodenum and of the sphincter, together with the pressure of liver bile, may be disadvantageous in such conditions. Previous administration of a small dose of atropine or traserin diminished this phenomenon somewhat both in power and duration, but did not abolish it.

The effects of normal and hypertonic saline solution on contractions of the sphincter and duodenum were so marked and so regular that it was possible to use this procedure for testing the effects of spasmolytic drugs on both structures.

SUMMARY

1. A method for simultaneously observing the activity of the factors most concerned with bile flow from the gall bladder has been described.

2. Sphincteric response can be independent of duodenal activity.

3. Normal or hypertonic saline administered intravenously induces prolonged periods of spastic contraction of the sphincter of Oddi and the duodenum which would constitute opposition to the flow of bile.

4. Glucose in distilled water, administered intravenously in isotonic or hypertonic concentrations, relaxes the duodenum and produces moderate contraction of the sphincter, which would offer little resistance to the flow of bile.

5. Glucose in normal saline, administered intravenously, produced an unpredictable effect, somewhat intermediate between the effect produced by either solution used alone.

6. The spasm producing effects of normal saline can be reduced or prevented by the use of atropine or traserin intravenously, whereas these drugs are without significant effect on the spasms induced by hypertonic saline. Nitroglycerine, amyl nitrite, and padutin, given intravenously were effective in temporarily relieving the spasms produced by hypertonic saline.

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CLINICAL STUDIES ON THE ANTIHEMORRHAGIC EFFECTS OF A NEW WATER-SOLUBLE VITAMIN K-LIKE SUBSTANCE

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THE discovery and isolation of vitamin K and the synthesis of substances having vitamin K-like activity constitute not only a triumph of modern chemistry but also an important advance in therapeutics. Before the discovery, only a few years ago, by Dam (8-11) of the specific fat-soluble substance called vitamin K, surgeons feared the aftermath of operations in obstructive jaundice, as obstetricians and pediatricians did the latent and active hemorrhagic diseases of the newborn, and clinicians the hemorrhagic diathesis of the cholemic state.

Dam and his coworkers are rightly credited with the discovery of vitamin K and also with postulating its economy in the animal organism. He designated the substance as the "loagulations" vitamin or vitamin K. Dam was guided to the discovery of the substance through his work on cholesterol and its possible synthesis by the hen. He had previously observed that the use of his experimental diet was followed by hemorrhages as well as by an erosive ulceration of the gizzard. The observations of Dam were soon confirmed by other workers and the literature became materially enriched and a rational basis was established for the clinical use of the substance. Almquist and Stokstad (2) were among the early workers on the problem and, simultaneous with, but independent of Dam, established the existence of vitamin K as a substance needed by the chick to maintain normal clotting time of blood.

Once the existence of vitamin K was definitely established, workers turned their attention to its isolation and synthesis. Early in 1939, Dam and his coworkers announced the isolation of vitamin K in a relatively pure form. This announcement was closely fol-

lowed by the publication of a report by Almquist and Klose (1) on the antihemorrhagic activity of synthetic 2-methyl-3-hydroxy-1, 4-naphthoquinone or phthiocol. They found that the physical and chemical properties of this compound simulated those known for vitamin K. In a letter to the editor of the *Journal of the American Chemical Society*, Binkley, MacCorquodale, Cheney, Thayer, McKee and Doisy (3) announced the preparation of the diacetates of dihydro vitamin K₁ and dihydro vitamin K₂ as further evidence that they had actually isolated both substances.

The syntheses of various quinones with vitamin K activity were announced in rapid succession. Among these was the tetra sodium salt of 2-methyl-1, 4-naphthohydroquinone diphosphoric acid ester which forms the basis for this report, and which for brevity will hereafter be referred to as preparation N-123. This substance was found by Foster, Lee and Solmssen (12) and by Almquist and Klose to possess on a molecular basis an activity much greater than that of methyl-naphthoquinone. It has been found in pharmacological studies that preparation N-123 has a wide margin of safety and adverse effects are absent in therapeutic doses.

The rationale of the clinical use of vitamin K and substances having vitamin K activity is the ability of such preparations to restore plasma prothrombin to normal levels. Vitamin K is absolutely essential for the coagulation of blood, and bile salts are necessary for the absorption of the substance from the intestinal tract. The clinical literature on the subject is rapidly expanding and published reports from various clinics are in agreement with our findings in the present study.

Butt, Snell and Osterberg (4, 5) found that the prolonged prothrombin time was reduced to within normal limits through the ad-

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TABLE I.—RESULTS WITH PREPARATION N 123-10 MILLIGRAM DAILY DOSE INTRAMUSCULARLY ADMINISTERED

No.	Patient	Diagnosis	Pre-operative %	Postoperative level						
				Medication period†					Post medication period	
				1st dose %	2nd dose %	3rd dose %	4th dose %	5th dose %	at last %	in
	T. R.	Carcinoma of colon with colostomy	79	84	80	79	79	7	71	75
	E. B.	Carcinoma of pancreas with liver metastases	73	100	8	100	80	90	100	100
	M. C.	Carcinoma of head of pancreas with jaundice	69	84	100	100	95	90		
	R. D.	Carcinoma of colon with metastases to liver	69	84	7	100	90	90	23	70
5	A. De	Carcinoma of pancreas with diabetes	75	84	90	94	90	100	100	100
6	E. H.	Common duct stone	90	8	100	100	100	100	100	100
	W. H.	Common duct stone and ascitis	68	73	76	79	100	100	100	100
8	C. J.	Acute cholecystitis with jaundice	76	84		88	7	90	100	100
	K. M.	Obstructive jaundice	70	93	80	81	100	100	100	100
10	J. M.	Obstructive jaundice with secondary complications	84	90	100	100	100	100	100	100
11	M. P.	Liver abscess	80	90	100	100	100	100	80	80
	J. P.	Obstructive jaundice with cirrhosis ‡	80	84	73	94	100	100	100	97
13	M. B.	Common duct stone and ascitis ‡	63	70	73	84	94	100	100	100
14	M. S.	Obstructive jaundice with slight biliary cirrhosis	61	80	73	84	100	90	100	100
16	A. T.	Carcinoma of pancreas, jaundice, urinary bladder infection	70	70	100	100	100	100	100	100
17	J. W.	Carcinoma of stomach and pyloric obstruction	90	80	70	90	100	100	73	75
19	F. W.	Cholelithiasis	76	80	66	90	73	100	100	100
23	C. W.	Empyema of gall bladder	73	80	76	90	100	100	100	100
26	D. T.	Intermittent obstructive jaundice with ascitis	48	100	100	87	87	70	100	100
27	O. B.	Carcinoma of liver	11	90	100	100	100	100	70	64

§ 48 and 72 hours respectively after last dose

† Lower values are at least 24 hours after dose

‡ Not done, no sign. All other doses no sign.

ministration of vitamin K and bile in their cases of obstructive jaundice. They observed that the administration of vitamin K concentrate with bile salts effectively prevented and controlled hemorrhagic diathesis, and that it made surgery in these patients less hazardous. Nygaard pointed out that transitory hypoprothrombinemia in the newborn may be prevented by the administration of vitamin K immediately after delivery. Scanlon and his coworkers tell of a case of obstructive jaundice in which postoperative bleeding occurred and which ceased following the administration of vitamin K. Smith and his coworkers reported that the use of vitamin K and bile salts effectively controlled postoperative bleeding in their cases. Butt, Snell and Osterberg (6) analyzed 63 cases studied at the Mayo clinic

during a period of 2 years and demonstrated the value of the preoperative use of vitamin K. Eight of the 63 cases did not receive preoperative doses of vitamin K and 5 of these patients developed postoperative bleeding.

Stewart (22) holds that dangerous hemorrhage may occur when plasma prothrombin concentration is less than 50 per cent of normal. He states that a mixture of vitamin K and bile salts will restore plasma prothrombin and control the tendency to hemorrhage. Cheney established the safety of intramuscular administration in man. Stewart and Allen observed a marked reduction in plasma prothrombin in cases of obstructive jaundice with biliary fistulas. They found a mixture of vitamin K and bile salts to give prompt improvement. Patients who did not

TABLE II.—RESULTS WITH PREPARATION N-123—10 MILLIGRAM DAILY DOSE ORAL ADMINISTRATION

No	Patient	Diagnosis	Prothrombin level							
			Pre limi- nary %	Medication period†					Post medication period	
				1st dose %	2nd dose %	3rd dose %	4th dose %	5th dose %	48 hrs * %	72 hrs * %
21	M P	Common duct stone, gall bladder removed	77	80	75	100	100	100	100	100
22	H R.	Common duct stone with jaundice	66	88	82	98	100	100	100	100
23	B K	Sepsis following gall bladder operation	30	58	76	65	80	51	50	50
24	S. J	Subdiaphragmatic abscess	65	100	85	83	100	100	85	85
25	J M	Peptic ulcer with gastroenterostomy	69	85	100	100	100	100	100	100
26	S N	Carcinoma of stomach with metastasis causing common duct obstruction	43	100	100	100	100	100	100	100
27	T N	Vitamin deficiency, alcoholism, early cirrhosis	50	85	100	100	100	100	100	100
28	G P	Ruptured appendix	33	75	88	90	100	100	94	100
29	E. S	Cirrhosis of liver	64	90	90	85	100	100	85	80
30	T S	Cirrhosis of liver (Banti's), hematemesis enlarged spleen	75	90	100	100	100	100	80	80
31	E. B	Carcinoma of head of pancreas	70	85	75	100	100	100	100	100
32	G V	Cirrhosis of liver with ascites	79	100	90	85	90	100	85	85
33	A W	Common duct stone	80	100	100	100	100	100	100	100
34	K. D	Common duct stone and diabetes	50	73	83	90	100	100	100	100
36	J N	Carcinoma of stomach with metastasis to liver	25	75	100	90	75	85	100	100
37	J S	Cirrhosis of Liver	30	69	70	75	100	100	75	65
38	W D	Chronic cholecystitis	55	75	85	100	100	100	100	100
39	F G	Carcinoma of pancreas with liver metastases	60	100	70	75	75	100	100	100
40	E H	Cirrhosis of liver	68	70	75	100	90	80	80	80
41	M K	Pericholecystic abscess with jaundice	60	100	100	100	100	100	100	100

*48 and 72 hours after last dose

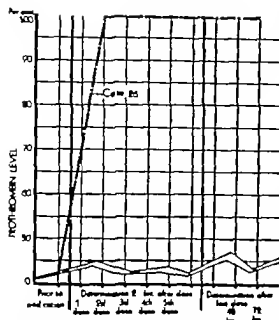
†Determination 24 hours after dose was administered

receive vitamin K before operation and who experienced severe postoperative bleeding were found without exception to have a plasma prothrombin concentration below 45 per cent Olson and Menzel reported on the use of vitamin K in 24 cases of obstructive jaundice They recommend the use of vitamin K and bile salts in all cases of jaundice, both before and after operation Rhoads and Fliegelman used a synthetic vitamin K preparation for the treatment of prothrombin deficiency in 10 patients, 9 of whom responded satisfactorily to the therapy Norcross and McFarland used a synthetic vitamin K preparation in 22 cases of hypoprothrombinemia They found that the substance effectively controlled bleeding except in the face of severe liver damage No toxic manifestations were observed

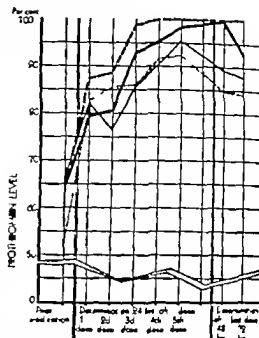
Kugelmass pointed out that severe cases of hemorrhagic disease in the newborn may be associated with prenatal transmission of the condition This has been shown by the lowered prothrombin content of the blood of the expectant mother He cited a number of such cases in which patients were successfully treated by the administration of vitamin K Poncher and Kato had 22 cases of hemorrhagic disease of the newborn successfully treated with synthetic preparations of vitamin K, prompt cessation of bleeding occurred and in no instance were transfusions needed

CLINICAL INVESTIGATION

This report summarizes our experiences with a vitamin K-like preparation, the tetra sodium salt of 2-methyl-1, 4-naphthohydroquinone diphosphoric acid ester or prepara-



Graph 1. Typical curve as obtained in patient with obstructive jaundice but without other complications



Graph 2. Variations in prothrombin level curves of patients with and those without liver disease or sepsis. Patients without liver disease or sepsis: Oral administration ———; subcutaneous administration — · — · —. Patients with liver disease or sepsis: Oral administration — · — · —; subcutaneous administration — · — · —.

tion N 123 in some 41 cases selected from the medical and surgical services of Cook County Hospital, Chicago. In most instances the patients represented cases of disease of the biliary tract or liver associated with jaundice. A small number of the cases studied had only gastro-intestinal disturbances or severe sepsis conducive to vitamin K deficiency.

A preliminary determination of the blood prothrombin levels according to the modified Smith method (24) was done on each patient. Then a daily dose of 10 milligrams of preparation N 123 was given over a period of 6 days. The blood prothrombin levels were determined daily for 8 days. On the seventh and eighth days, the clotting time was also determined.

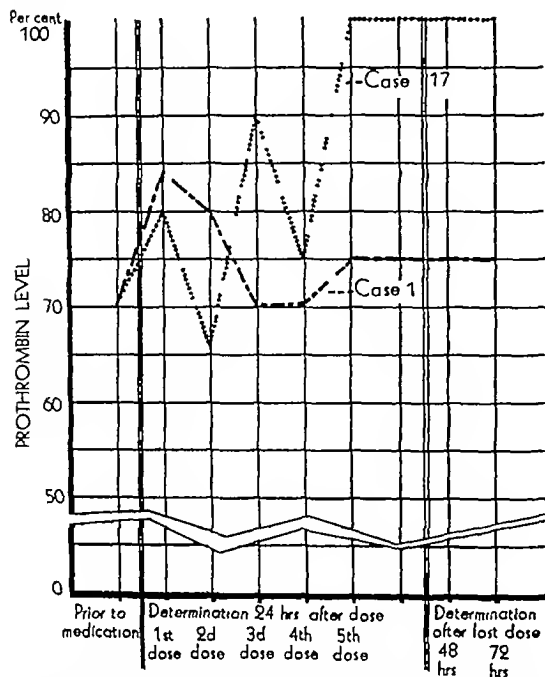
METHOD OF PLASMA PROTHROMBIN DETERMINATION

Rabbit brains and lungs are used as a source of thromboplastin. They are macerated in a mortar. Normal saline solution is then added and the material is placed in the ice box where it is permitted to stand for 3 hours. The supernatant fluid is decanted and strained through gauze. Usually the solution is centri-

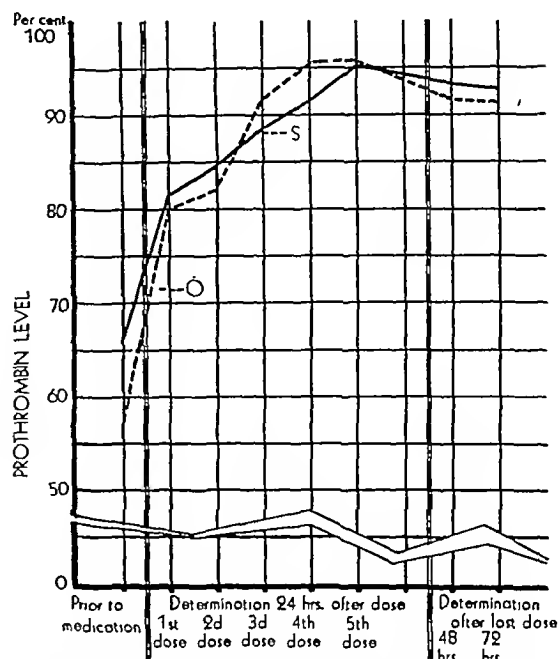
fuged. The thromboplastin is kept in the ice box, and it is considered advisable to warm the sample of thromboplastin to room temperature before it is used. Because of the rapid deterioration in the activity of thromboplastin, a normal prothrombin time for the sample must be determined daily.

A stop watch is used to insure accuracy in obtaining the clotting time. One-tenth thromboplastin is placed in a serological tube. To this is added 0.7 cubic centimeter of blood, drawn quickly and automatically. The time is recorded in seconds from the time the blood contacts the thromboplastin until the time the clot appears in the tube. The tube is slowly inverted until clotting occurs. A normal individual is tested several times to obtain a correct normal clotting time against which patients are checked.

Normal plasma prothrombin time in seconds
Patient's plasma prothrombin time in seconds — per
cent of clotting activity



Graph 3 Bizarre prothrombin level curves obtained in patients with deficient food intake and deficient absorption (pyloric obstruction, colostomy)



Graph 4 Curves showing response in prothrombin level to oral, O, and subcutaneous, S, administration of preparation N-123

A prolonged prothrombin time in seconds will give a low percentage of clotting activity. Levels below 70 per cent are to be considered dangerous, and hemorrhage may occur when such levels are reached.

Of the 41 patients in our series, 21 received a daily dose of 10 milligrams of preparation N-123, subcutaneously while 20 were given the substance per os. Of this latter group, 10 patients took the N-123 in combination with 5 grains of bile salts. The other patients did not receive any bile salts. In a small group of patients, blood prothrombin levels were determined hourly after injection of the initial 10 milligram dose. This was to determine just how rapidly the prothrombin levels rise after the patient receives the medication.

RESULTS WITH PREPARATION N-123

In most of our cases, the prothrombin level rose to normal limits within 24 to 48 hours after the initial dose of preparation N-123. After the 100 per cent level was reached and held by the daily dose, it could be maintained

for 48 to 72 hours after the medication was discontinued. Exceptions to the foregoing occurred in a number of instances, for example when aggravation of an existing jaundice or other condition caused fluctuations (up and down) in the prothrombin level even during the period of medication. Lag or fluctuation in the response to the medication occurred also in cases with sudden appearance of high fever, profuse vomiting, or starvation. In the face of existing liver damage, a definite lag in the rise of the prothrombin level was observed, and in a few cases never reached 100 per cent, also prothrombin levels could not be maintained after medication was stopped.

Patients with pyloric obstruction, or after colostomy, or with severe sepsis and the attending starvation, present a response similar to that found in cases with liver damage. Infection plus liver damage was found markedly to retard response to the therapy. In one case the prothrombin level did not rise above 80 per cent. In a number of cases of jaundice complicated by sepsis, the prothrombin levels

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CULTIVATION of bacteria from the blood was first used for the study of infections due to anthrax bacilli, plague bacilli, and hemolytic streptococci. As a result of this early experience with highly invasive bacteria a positive blood culture report has been accorded undue clinical significance with connotations as to bacterial virulence and absence of host resistance. The demonstration of viable bacteria in the circulating blood is important only in relation to the kind of bacteria found and the pathological anatomy of the lesion which permitted the breaking down of the normal barrier to blood stream contamination.

A *sustained bacteriemia*, often referred to by the vague term of "septicemia," is characterized by the isolation of invasive bacteria of high virulence in relatively constant numbers per cubic centimeter of blood, a nonsuppurative cellulitis at the portal of entry and evidence of lymphatic transmission of the infection. Distinct from such blood stream infection is blood stream contamination by the *intermittent bacteriemia* of septic phlebitis or endocarditis which is characterized by a variable number of bacteria per cubic centimeter of blood, a peripheral or visceral focus of localized infection and complete absence of signs of lymphangitis. The organisms responsible for this latter type of bacteriemia need not possess any great invasive ability.

The importance of thrombophlebitis in the production of metastatic abscesses was recognized by John Hunter. Purulent phlebitis of major veins is an accepted complication of otitic and puerperal infections but septic thrombophlebitis of minor venous radicles as a cause of bacteriemia has received infrequent pathological (36) and clinical (16, 22, 32, 33, 37) consideration. In such papers it is made evident but not emphasized that the staphylococcus is the etiological organism found most

frequently in bacteriemias arising from septic thrombophlebitis of minor venous radicles.

Academic researches upon staphylococcal infection have been more definitive. The staphylococci are of limited invasiveness and cannot maintain a phase in which the organisms are resistant to phagocytosis (19). The staphylococcal exotoxins are more poisonous for animals (5, 6, 7) than for human beings (34, 35, 39, 40). Further, toxigenicity is not a criterion of invasiveness as may be recalled by tetanus and diphtheria. The tissue response to staphylococcal infection is associated with prompt lymphatic obstruction and subsequent thrombosis of the vascular capillaries (24-31). This sort of evidence has led Topley to conclude that in a bacteriemic staphylococcal infection "the cocci are carried from the original focus of infection in detached fragments of an infected thrombus."

Final acceptance of this verdict would seem to depend upon its confirmation in clinical observations. The constancy of a suppurative focus in staphylococcal bacteriemia is a surgical axiom. Occasionally the bacteriemia complicates a peripheral lesion such as a boil or a carbuncle. More frequently the local focus is in the bone, brain, kidney, or endocardium, and there is no demonstrable portal of entry. Thus there is good ground for believing that an initial bacteriemia arising from a peripheral lesion is frequently asymptomatic but permits the implantation of bacteria in vulnerable organs. The staphylococcemic phase associated with visceral abscesses must necessarily be a recurrent bacteriemia related to the active visceral focus and independent of the healed or forgotten peripheral lesion. Figures 1 to 5 present evidence of the occurrence of septic thrombophlebitis in minor vascular radicles of various viscera from patients with bacteriemic staphylococcal infection.

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reached normal only after about 96 hours. It is interesting to note that in some of these the prothrombin levels could be maintained for 48 hours after stopping the medication.

In our hands, cases of K-avitaminosis resulting from uncomplicated obstructive jaundice were found to respond promptly to preparation N 123 10 milligrams daily whether given parenterally or per os (Graph 1). In face of liver damage and resulting interference with vitamin K storage and utilization and in those cases with sepsis and gastrointestinal pathology (pyloric obstruction, colitis etc.) in which absorption is also impaired the response to the medication is less prompt, less complete and for a shorter period of time (Graphs 2 and 3). This observation is, of course in agreement with that of other clinicians. Naturally the degree of hypoprothrombinemia, the condition of liver parenchyma, the state of the gastrointestinal tract and the absorption mechanism (when given per os) all play a rôle in the anti-hemorrhagic effect of any preparation possessing vitamin K-like activity.

It has been our observation that when the functional integrity of the liver is not greatly disturbed impairment of vitamin K absorption as seen in certain gastrointestinal conditions and in sepsis is followed by hypoprothrombinemia only after a prolonged period of such impairment. A nearly normal prothrombin level was found in several instances of colitis, complicated peptic ulcer etc. where K-avitaminosis was suspected because of small intake of food for a long period. However in cases with liver parenchyma damage a markedly decreased prothrombin level is nearly always present. Lowest prothrombin levels are found in cases of sepsis with liver damage and sepsis with obstructive jaundice.

SUMMARY AND CONCLUSIONS

The 2-methyl-4-naphthohydroquinone diphosphoric acid ester tetra sodium salt, referred to as preparation N 123 a synthetic substance having vitamin K-like activity was used in 41 cases. Satisfactory results attended its administration. The substance has been found to be more active on a molecular basis, than methyl-naphthoquinone.

A daily dose of 10 milligrams, parenterally or per os, was found capable of raising prothrombin levels to normal within 24 to 48 hours. In many instances the normal level can be maintained for 24 to 72 hours after the medication has been stopped.

As is generally true of vitamin K preparations, the effectiveness of the substance is partially diminished in the face of liver parenchyma damage, gastrointestinal disturbances, or sepsis. The presence of any two of these factors calls for continuous administration of the preparation to maintain the prothrombin level.

Despite the fact that our patients were mostly far advanced and complicated cases, the results obtained by the use of preparation N 123 were quite satisfactory (Graph 4), even though the curves do not show such steep rise as seen in the uncomplicated cases (Graph 1).

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Fig. Pathology No. 32-794 A. Septic thrombophlebitis in the metaphyseal focus of osteomyelitis.

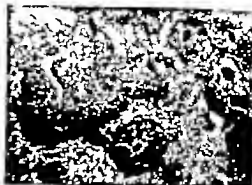


Fig. 1. Pathology No. 70. Kidney abscess with blood vessel occluded by septic thrombus.

cause of death. The material has been analyzed in Table I. The first group contains the instances of suppurative phlebitis of major venous pathways. Deaths occurred as the result of direct extension of the thrombus to vital venous channels or as the result of massive pulmonary infarction. It is noteworthy that multiple visceral abscesses did not occur and that the lesions were confined to the involved veins and the lungs. The second group contains the instances of endocarditis. The classical pattern of peripheral and visceral infarction occurred with left endocarditis. Deaths from right endocarditis were attributable to the massive pulmonary infarction necessarily incident to such a lesion. The third group had in common one or more foci of abscess formation in the lungs and a pattern of peripheral and visceral infarction and supuration which was entirely comparable to that seen as a result of left endocarditis. Death was not attributable to the lung lesions but rather to the peripheral and visceral metastases propagated from the pulmonary thrombophlebitis incident to supuration of the septic lung infarcts. Myocardial abscesses occurred predominantly in this group. There were 2 cases with true petechiae and 4 instances of sterile visceral infarction. The fourth and last group of patients includes those with brain abscess and requires no discussion as to cause of death. It does not appear necessary to presuppose a retrograde contamination of the vertebral venous plexus from the caval system (2) to explain these abscesses.

Table II records the incidence of septic metastases to vital organs. Abscesses of the myocardium deserve special comment. Abscesses of the subendocardial portion of the myocardium may be followed by septic mural thrombi whereas abscesses of the myocardial periphery may be followed by pericarditis. Rupture of the heart through such an abscess is a recognized complication of the drainage of a staphylococcal pericarditis.

Table III summarizes the presumptive portals of entry in the reported cases. Abscesses or carbuncles, sinusitis, and prostatic infection were the chief known initial lesions. The incidence of prostatic infections is a reflection of the vulnerability to thrombophlebitis of the prostatic venous plexus. In the diagnosis of primary staphylococcal pneumonia it is important to remember that a septic pulmonary infarct may simulate pneumonia and still be the first clinical symptom of a visceral abscess.

The importance of pulmonary thrombophlebitis in staphylococcal bacteremia is emphasized in the following case report.

An adolescent girl (Case No. 228574, 7 years of age) entered with an acute osteomyelitis of the upper end of the tibia and a sustained temperature of 5 degrees F by rectum. Incision and drainage of the subperiosteal abscess was followed by intensification of her symptoms, pain in the chest, and pleural friction rub. A femoral vein ligation was performed in the hope of preventing further pulmonary infarction. Coincidental cultures of blood from the femoral and antecubital veins failed to show conclusive evidence of a more intense contamination of the blood from the osteomyelitic focus.

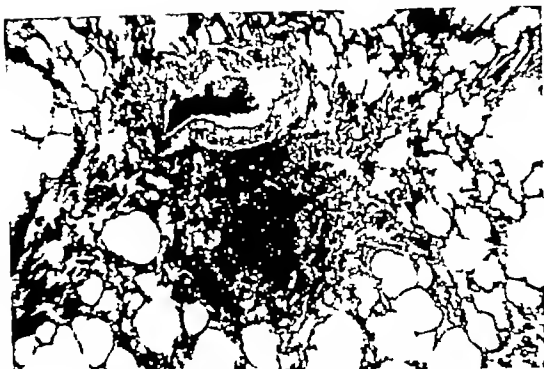


Fig 3 Pathology No 6208 Septic thrombophlebitis in the lung

There were no demonstrable emboli in the smear of the femoral blood. As is shown in Table IV there was a prompt reduction in the number of colonies of staphylococci in the peripheral blood after ligation of the femoral vein, and this was correlated with clinical improvement and a reduction of temperature. Four days after ligation of the femoral vein the temperature rose again, the patient became more severely ill and an intensification of the bacteremia was noted. This was correlated with a more definite friction rub, râles, purulent sputum containing staphylococci, and an increase in the respiratory rate to 40 per minute. Portable x-ray films were not completely satisfactory but failed to show a recognizable abnormality. The intensity of the bacteremia gradually diminished as the pulmonary signs and symptoms subsided. Urine cultures were consistently negative for staphylococci. The subsequent convalescence was uneventful except for a sequestrectomy, and the patient has failed to show any new foci during the 10 months since discharge. In retrospect it is felt that this patient entered with a bacteremia incident to her osteomyelitis. This was arrested by femoral vein ligation after septic lung infarcts had occurred. A recurrent bacteremia was associated with suppuration of the pulmonary infarcts as evidenced by pus in the sputum. It is important that these lung abscesses healed spontaneously.

Examination of this material has convinced me that staphylococcemia is dependent upon an intravascular focus of infection. It follows that every effort should be made in the management of staphylococcal abscesses to define the diagnostic features of septic thrombophlebitis in the stage before significant metastasis occurs. It is my clinical impression that a total white blood cell count of 15,000 or over is strongly suggestive of intravascular sepsis. Positive evidence of septic thrombophlebitis is given by a chill, a sudden spike of fever to



Fig 4 Pathology No 7010 Beginning organization of a septic thrombosis of a vessel in the lung

103 degrees F or more, a pulmonary infarct, a positive blood culture, or a palpably thrombosed vein. Septic pulmonary infarcts may simulate pneumonic consolidation so closely that it is a common clinical error to label such lesions as "bacteriemic staphylococcal pneumonia." Such "pneumonias" are often the first clinical symptom of a peripheral visceral abscess, particularly vertebral osteomyelitis, or right sided endocarditis. This latter diagnosis has been made clinically by the demonstration of multiple pulmonary infarcts in bacteriemic patients with no demonstrable peripheral or visceral focus of infection.

Scott (37) has expressed the opinion that the surgical drainage of pus under pressure is the procedure of choice in treatment of the infected vascular bed. This is sound doctrine.

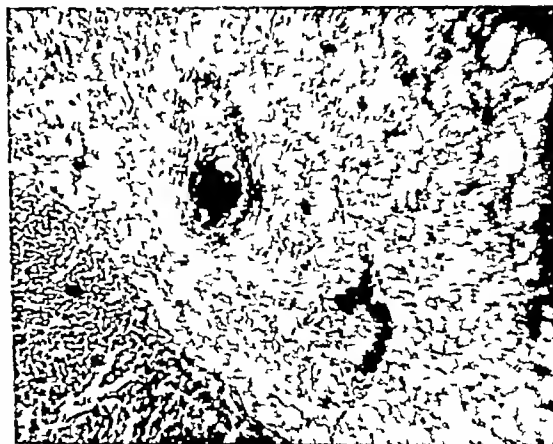


Fig 5 Pathology No 6007 Septic thrombus in a vessel in the heart

TABLE I.—DEATHS FROM STAPHYLOCOCCAL BACTEREMIA

	No. deaths	Total no. deaths
I. Thrombophlebitis and phlebothrombosis of major venous paths:— Deaths due to extension to intra-cranial venous sinuses.	5	8
b. Death due to caval extension Deaths due to mesent. septic infarction of the lungs	—	
II. Endocarditis a. Patients with left endocarditis, only one of whom showed proximal pulmonary abscess.	6	3
b. Patients with right endocarditis Patients with bilateral endocarditis	—	
III. Septic lung infarcts not secondary to endocarditis Patients with frank pulmonary abscesses and multiple peripheral lacunar abscesses.† of these patients showed patchiness	—	—
b. Patient with bronchopneumonia and myocardial abscess	—	
c. Patient with prostatic pneumonia, thrombophlebitis, lung infarct and myocardial abscess	—	
IV. Brain abscess a. Patient entered with carbuncle of the neck and dard of brain abscess and meningitis	—	—
b. Patient entered with brain abscess and showed subsequent septic infarcts of lung	—	
Total		23

but does not always prove effective. Persistent leucocytosis, fever, chills or positive blood cultures have occasionally led me to excise the inflammatory focus with subsequent prompt control of the infection.

Neuhof (32, 33) and Meleney (22, 23) are advocates of ligation or excision of veins to control purulent phlebitis in a surgically accessible vein. Obviously this method cannot be applied to intracranial venous sinuses or pulmonary veins.

TABLE II.—INCIDENCE OF SEPTIC METASTASES IN VITAL ORGANS DISCOVERED AT AUTOPSY

Location	No. cases
Lung	23
Myocardium	
Kidney	
Brain and spinal cord	

The intravenous injection of immune sera has appealed to many clinicians. Blair has recently completely reviewed the problem of staphylococcal pathogenicity and immunity. On the basis of factual experimental data complicated by clinical impressionism it would appear that "within a definitely circumscribed area the injurious action of the coed and their products may be intense and their capacity far outweighs any ability to produce toxin. Antitoxic immunity may prolong life in animals susceptible to the toxin but such immunity does not afford complete protection to infection. The existence of an antibacterial immunity has never been proved and I have been unable to correlate the presence of agglutinins with eventual recovery (Table V) although Valentine and Butler (40) thought that blood stream clearance of bacteria occurred more rapidly in the presence of such agglutinins. Undoubtedly many staphylococci are destroyed in patients that survive a staphylococcal bacteremia. The nonspecific bactericidal ability of cells in the lungs, liver and spleen should not be forgotten as a part of the normal clearance mechanism.

Table VI summarizes the mortality statistics for untreated and variously treated staphylococemic infections. Such data are almost worthless because they are based upon the entirely false assumption that staphylococcal bacteremia is a disease entity within itself. A reduction of the mortality rate from 75 per cent to 30 per cent may be statistically significant but it is far from the ideal mortality rate that might be anticipated with a specific antibacterial agent. It is significant that the intravenous injection of any of several foreign chemical substances appears to be effective in lowering the mortality rate. Meleney's (22) bacteriophage is prepared in a yeast extract broth and yeast nucleic acid is known to increase the nonspecific resistance to staphylococcal infection (3, 13). The bar-

TABLE III.—PORTALS OF ENTRY

Primary infection	No. cases
Abscess	6
Carbuncle	4
Stomatitis	4
Pharyngitis	
Prostatic abscess or postoperative infection	4
Unknown	3

TABLE IV—BACTERIOLOGICAL STUDY OF THE BACTERIEMIC PHASE IN A FEMALE

Clinical notes	Date	Source of culture	Time	Colonies per c cm blood		
				0.5 c.cm	1 c.cm	2 c.cm
	Dec. 26	Antecubital vein	a.m.		20	
Incision and drainage subperiosteal abscess	Dec. 27					
	Dec. 28	Antecubital vein	a.m.		132	
Ligation of femoral vein	Dec. 29	Antecubital vein	12.30 p.m.	16	25 and 28	31
		Femoral vein	12.30 p.m.	10	28 and 40	62
		Antecubital vein	3.00 p.m.	11	7	12
		Antecubital vein	5.00 p.m.	4	2	7
	Dec. 30	Antecubital vein	10.00 a.m.	0	2	1
	Dec. 31				Positive culture only from 5 c.cm of blood	
	Jan. 1					
Increase of pulmonary symptoms	Jan. 2	Antecubital vein	a.m.	9	14	38
	Jan. 3	Antecubital vein	a.m.	4	5	7
	Jan. 4	Antecubital vein	a.m.	1	1	1
	Jan. 8	Antecubital vein	a.m.	0	1	1
Convalescent	Jan. 10	Antecubital vein	a.m.		Sterile	

den of proof is quite clearly upon Meleney to exclude this nonspecific factor in view of the overwhelmingly adverse evidence afforded by animal experiments on bacteriophage therapy.

The importance of a nonspecific enhancement of resistance to staphylococcal infection is well illustrated by the experiments of Cowan in which active immunization with staphylococci or with a totally unrelated organism, *Pasteurella pseudotuberculosis*, was equally effective in increasing the survival rate of experimentally infected rabbits. The mechanism whereby nonspecific shock reactions increase resistance to staphylococcal infection is unknown and has never been shown to be due to a specific immune body. Peptone shock in dogs is followed by a prolongation of

the clotting time of the blood which has been correlated with an increased heparin content of the plasma and a disappearance of the meta-chromatic granular material of the Ehrlich

TABLE VI—MORTALITY STATISTICS IN STAPHYLOCOCCAL BACTERIEMIA

	Total	Survived	Died	Per cent died
With surgical drainage and transfusions				
Joyner and Smith (14)	16	8	8	50
Baker and Shands (1)	30	9	21	70
Longacre, Zaytzeff-Jern, and Meleney (18)	54	10	44	81
	100	27	73	73
With antitoxin				
Joyner and Smith (14)	13	11	2	15
Dolman (10)	64	29	35	55
Baker and Shands (1)	35	26	9	26
	112	66	46	41
With bacteriophage				
Lawson (17)	38	7	31	82
Scott (37)	8	4	4	50
MacNeal and Frisbee (21)	15	7	8	53
MacNeal and Frisbee (21)	100	25	75	75
Lutton (12)	7	6	1	14
Meleney (before 1936) (22)	15	4	11	73
Meleney (1936-1938) (22)	21	15	6	29
	204	68	136	70
With antibacterial serum				
Cadham (8)	10	9	1	10
Julianelle (15)	17	7	10	59
	27	16	11	41

TABLE V—RELATIONSHIP BETWEEN PRESENCE OF AGGLUTININS AND OUTCOME

Probable focus	Agglutinins*	Antitoxin†	Result
Furuncle of hand	++++	Yes	Died
Carbuncle of face	++++	Yes	Died
Endocarditis	++	Yes	Died
Osteomyelitis	++	No	Died
Phlegmon abdominal wall	0	Yes	Died
Osteomyelitis	0	No	Survived
Osteomyelitis	0	No	Survived

*Antibacterial antibody as developed by patient and determined by slide agglutination (10)

†Commercial antitoxin 100,000 units injected intravenously

TABLE I.—DEATHS FROM STAPHYLOCOCCAL BACTERIEMIA

	No. deaths	Total no. deaths
I. Thrombophlebitis and phlebothrombosis of major venous pathways Deaths due to extension to intracranial venous sinuses	5	8
b. Death due to caval extension	—	—
c. Deaths due to massive septic infarction of the lungs	—	—
II Endocarditis a. Patients with left endocarditis, only one of whom showed prodromal pulmonary abscess	6	—
b. Patients with right endocarditis	3	—
c. Patients with bilateral endocarditis	—	—
III. Septic lung infarcts not secondary to endocarditis Patients with frank pulmonary abscesses and multiple peripheral visceral abscesses. Two of these patients showed petechiae	—	—
b. Patient with bronchopneumonia and myocardial abscess	—	—
c. Patient with prostatic plasma thrombophlebitis, lung infarct and myocardial abscess	—	—
IV Brain abscess a. Patient entered with carbuncle of the neck and died of brain abscess and meningitis	—	—
b. Patient entered with brain abscess and showed subsequent septic infarcts of lung	—	—
Total	—	23

but does not always prove effective. Persistent leucocytosis, fever chills, or positive blood cultures have occasionally led me to excise the inflammatory focus with subsequent prompt control of the infection.

Neuhof (32, 33) and Meloney (22, 23) are advocates of ligation or excision of veins to control purulent phlebitis in a surgically accessible vein. Obviously, this method cannot be applied to intracranial venous sinuses or pulmonary veins.

TABLE II.—INCIDENCE OF SEPTIC METASTASES IN VITAL ORGANS DISCOVERED AT AUTOPSY

Location	No. cases
Lung	28
Myocardium	—
Kidney	—
Brain and spinal cord	—

The intravenous injection of immune sera has appealed to many clinicians. Blair has recently completely reviewed the problem of staphylococcal pathogenicity and immunity. On the basis of factual experimental data uncomplicated by clinical impressionism it would appear that 'within a definitely circumscribed area the injurious action of the cocci and their products may be intense and 'this capacity far outweighs any ability to produce toxin. Antitoxic immunity may prolong life in animals susceptible to the toxin but such immunity does not afford complete protection to infection. The existence of an antibacterial immunity has never been proved and I have been unable to correlate the presence of agglutinins with eventual recovery (Table V) although Valentine and Butler (40) thought that blood stream clearance of bacteria occurred more rapidly in the presence of such agglutinins. Undoubtedly many staphylococci are destroyed in patients that survive a staphylococcal bacteremia. The nonspecific bactericidal ability of cells in the lungs, liver and spleen should not be forgotten as a part of the normal clearance mechanism.

Table VI summarizes the mortality statistics for untreated and variously treated staphylococcal infections. Such data are almost worthless because they are based upon the entirely false assumption that staphylococcal bacteremia is a disease entity within itself. A reduction of the mortality rate from 75 per cent to 30 per cent may be statistically significant but it is far from the ideal mortality rate that might be anticipated with a specific antibacterial agent. It is significant that the intravenous injection of any of several foreign chemical substances appears to be effective in lowering the mortality rate. Meloney's (22) bacteriophage is prepared in a yeast extract broth and yeast nucleic acid is known to increase the nonspecific resistance to staphylococcal infection (3, 13). The bar

TABLE III.—PORTALS OF ENTRY

Primary infection	No. cases
Abscess	6
Carbuncle	4
Sore throat	4
Pneumonia	—
Prostatic abscess or postoperative infection	4
Unknown	3

TABLE IV—BACTERIOLOGICAL STUDY OF THE BACTERIEMIC PHASE IN A FEMALE

Clinical notes	Date	Source of culture	Time	Colonies per c.cm blood		
				0.5 c cm	1 c cm	2 c cm
	Dec 26	Antecubital vein	a m		20	
Cision and drainage subperiosteal abscess	Dec 27					
	Dec. 28	Antecubital vein	a m		132	
igation of femoral vein	Dec 29	Antecubital vein	12 30 p m	16	25 and 28	31
		Femoral vein	12 30 p m	10	28 and 40	62
		Antecubital vein	3 00 p m	11	7	12
		Antecubital vein	5 00 p m	4	2	7
	Dec 30	Antecubital vein	10 00 a m	0	2	1
	Dec 31				Positive culture only from 5 c cm of blood	
	Jan 1					
crease of pulmonary symptoms	Jan 2	Antecubital vein	a m	9	14	38
	Jan 3	Antecubital vein	a m	4	5	7
	Jan 4	Antecubital vein	a m	1	1	1
	Jan. 8	Antecubital vein	a m	0	1	1
onvalescent	Jan 10	Antecubital vein	a m		Sterile	

len of proof is quite clearly upon Meleney to exclude this nonspecific factor in view of the overwhelmingly adverse evidence afforded by animal experiments on bacteriophage therapy.

The importance of a nonspecific enhancement of resistance to staphylococcal infection is well illustrated by the experiments of Cowan in which active immunization with staphylococci or with a totally unrelated organism, *Pasteurella pseudotuberculosis*, was equally effective in increasing the survival rate of experimentally infected rabbits. The mechanism whereby nonspecific shock reactions increase resistance to staphylococcal infection is unknown and has never been shown to be due to a specific immune body. Peptone shock in dogs is followed by a prolongation of

the clotting time of the blood which has been correlated with an increased heparin content of the plasma and a disappearance of the meta-chromatic granular material of the Ehrlich

TABLE VI—MORTALITY STATISTICS IN STAPHYLOCOCCAL BACTERIEMIA

	Total	Survived	Died	Per cent died
With surgical drainage and transfusions				
Joyner and Smith (14)	16	8	8	50
Baker and Shands (1)	30	9	21	70
Longacre, Zaytzeff, Jern, and Meleney (18)	54	10	44	81
	100	27	73	73
With antitoxin				
Joyner and Smith (14)	13	11	2	15
Dolman (10)	64	29	35	55
Baker and Shands (1)	35	26	9	26
	112	66	46	41
With bacteriophage				
Lawson (17)	38	7	31	82
Scott (37)	8	4	4	50
MacNeal and Frisbee (21)	15	7	8	53
MacNeal and Frisbee (21)	100	25	75	75
Dutton (12)	7	6	1	14
Meleney (before 1936) (22)	15	4	11	73
Meleney (1936-1938) (22)	21	15	6	29
	204	68	136	70
With antibacterial serum				
Cadham (8)	10	9	1	10
Juhanelle (15)	17	7	10	59
	27	16	11	41

TABLE V—RELATIONSHIP BETWEEN PRESENCE OF AGGLUTININS AND OUTCOME

Probable focus	Agglutinins*	Antitoxin†	Result
Furuncle of hand	++++	Yes	Died
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Phlegmon abdominal wall	o	Yes	Died
Osteomyelitis	o	No	Survived
Osteomyelitis	o	No	Survived

*Antibacterial antibody as developed by patient and determined by slide agglutination (10)

†Commercial antitoxin 100 000 units injected intravenously

mast cells of the liver (41). Such an auto-heparinization might prove beneficial to a patient with bacteriemia arising from a septic thrombophlebitis. The successful treatment of 2 cases of bacteriemic staphylococcal thrombophlebitis of the cavernous sinus has been attributed to a combination of chemotherapy and heparin (20).

ANALYSIS OF STUDY

Bacteriemic staphylococcal infection has been analyzed from clinical and autopsy material. The weight of evidence favors the hypothesis first emphasized by Adams, Welch, and Virchow that the bacteriemia arises from an intravascular focus of infection. Such foci may occur as purulent phlebitis of major veins, as septic thrombophlebitis of minor venous radicles in and around a localized suppurative lesion or as primary endocarditis. Septic pulmonary infarction with subsequent abscess formation is followed by peripheral infarctions which make it appear that septic pulmonary thrombophlebitis may be comparable to left endocarditis.

Such a conception of the source and pattern of staphylococemia has a broad implication for successful therapy. Intravascular extension of a staphylococcal infection should be suspected in the presence of a leucocytosis of 15,000 or more, a chill, a sudden spike of fever to 103 degrees F or over, a pulmonary infarct, a palpably thrombosed vein or a positive blood culture. A direct attack upon the inflammatory focus may be made by excision of inflammatory foci, drainage of pus or venous ligation. The recognition of the bacteriemia as a complication of a localized inflammatory process makes it unlikely that immune serum or bacteriophage can at the present time supplant surgical treatment. The clinical results of treatment with antitoxin, antibacterial antibody, and bacteriophage do not suggest that such therapy is specific and it is entirely possible that such success as has been reported may be due to a nonspecific enhancement of resistance.

CONCLUSIONS

1. Staphylococemia has been presented as arising from intravascular foci of infection.

2. Pulmonary thrombophlebitis has been considered as a factor in the perpetuation of a staphylococcal bacteriemia.

3. Metastatic abscesses follow a pattern consistent with septic infarctions.

4. Varied surgical management is important in the treatment of bacteriemic infection.

5. It is not clear that antibacterial serum, antitoxin or bacteriophage have made a specific antibacterial effect in treatment of staphylococemia.

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CARCINOMA OF THE ESOPHAGUS

Torek's Operation, Recovery

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ENCOURAGED by the enthusiastic and effective work of surgeons of the United States — Franz Torek, Willy Meyer, Libenthal, Eggers, Hedblom, Garlock, Adams, King, Marshall, Ochsner, DeBakey, Churchill, Alexander, Scott, Ogilvie, Whipple, and Cartell—we faced the problem of the surgical treatment of carcinoma of the esophagus, and, although we failed in our first ten attempts, we finally succeeded in working out the technique described here

Doubtless a decisive factor in the success of this technique described is the previous pneumothorax operation as originated by Arce. This technique has been employed by him and by us since 1919. It makes intrathoracic maneuvers easier not only for the operator but for the patient. We have had a large experience with this operation, especially in the treatment of tumors of the lungs and of the thoracic wall.¹

¹Ivanissevich, Egües y Fernandez J. C., Técnica precisa para extirpar los tumores parietales del torax emergentes en la cavidad pleural. Bol y trab Soc de cirug de Buenos Aires 1938 22 925. Bol. inst de clin quir 1939 123 5. Rev Asoc méd argent. 1939 52 404.

In our patient, we used spinal anesthesia with metycaine. We believe that spinal and general anesthesia with cyclopropane are usually recommended for this operation.

R. G., 87,887 of the Instituto de Clínica Quirúrgica, chair of professor Arce, M. D.

Lorenzo Tarpin, aged 52 years, laborer, Argentinian, who lived in General Pico F. C. S., province of Buenos Aires, came to the institute on September 27, 1940. His illness had begun 2 months previously with manifestations of mechanical dysphagia, noticeable at first in efforts to swallow solid foods. The first symptom he noticed was the detention of a bit of meat in the upper part of the esophagus. Twenty-four hours later the bit of macerated meat was expelled by the mouth. The sensation of a foreign body then disappeared and the passage of food was partially re-established.

This episode was repeated several times, however. The arrest of the nutritious bolus in the esophagus produced pain of moderate intensity, which disappeared once the



Fig 1. Roentgenogram showing defect at the level of the middle third of the esophagus.

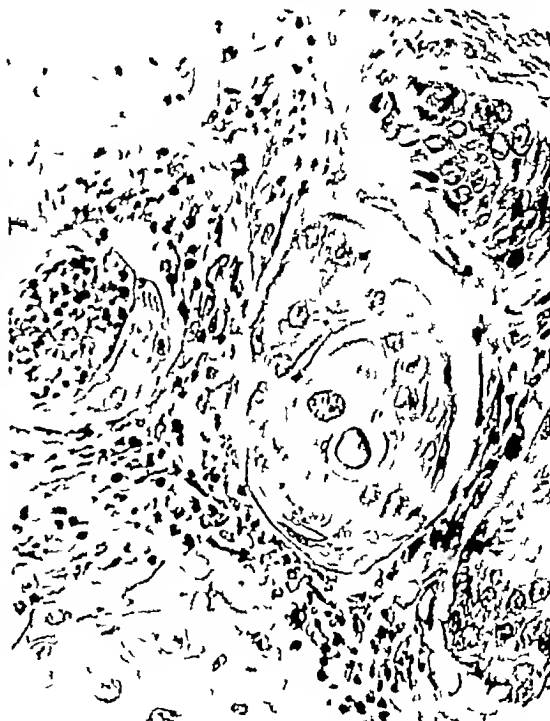


Fig 2. Photomicrograph showing basocellular epithelioma.



Fig. 3 Left posterolateral thoracotomy

food was expelled. Likelihood could be swallowed normally. The swallowing of solids became more and more difficult, and the patient's general condition grew considerably worse. He lost more than 50 pounds in eight to nine months.



Fig. 4 The soft parts between the rib removed, the pleural space is opened. The space between the pleura that covers the aorta is opened, b, esophagus, c, incision of



Fig. 4 Wide costal resection.

His family and personal history was without importance. He was not an alcoholic and smoked in moderation.

The clinical examination showed no external evidence of disease. He was tall man, well proportioned, of long bones, and had become much thinner. The muscular masses were moderately well developed. The teeth were in very bad condition both as to hygiene and conservation. There were no cervical glands. The respiratory and circulatory apparatus were in normal condition. The abdomen was normal. The roentgenographic examination, carried out when he entered the hospital, showed characteristic change of incomplete stricture at the level of the middle third of the esophagus (Fig. 5).

On September 25, 1940, performed an esophagotomy which revealed at 37 centimeters from the dental arch an obstruction which consisted of fleshy mass and which filled two-thirds of the lumen of the organ. Examination of tissues removed showed basocellular epithelioma (Dr. Niles, September 30, 1940) (Fig. 6).

The blood analysis showed red blood cells, 5,230,000; white blood cells, 8,400; hemoglobin, 16.43 grams (95 per cent); globular albumin, 9.0; volumetric index, 20; sedimentation index, 0.9; anisocytosis, slightly marked. Wassermann reaction was negative. Kahn reaction, negative. Coagulation time, 44.4 minutes; bleeding time, four and five minutes. Polymorphonuclear neutrophils numbered 67 per cent, polymorphonuclear eosinophils, per cent, lymphocytes, 5 per cent, monocytes, 7 per cent (Dr. Niles, September 3, 1940). Chemical blood analysis revealed urea, 30; glucose, grams per 100.

October 2, 1940, Professor Arce performed gastrostomy following his own technique.

October 7, performed the first stage of a pneumothorax (Arce). Three hundred cubic centimeters of air was introduced in the left pleura, the patient remained in the operation position. On October 12, the second stage of the pneumothorax was performed, 100 cubic centimeters of air was introduced in the right pleura. Patient tolerated operation. On October 15, showed total collapse of the lungs. On October 16, showed total collapse of the lungs. On October 17, showed total collapse of the lungs.



Fig 6 Mobilization of the infra aortic esophagus, marked by dotted line

On October 31, 1940, with the assistance of Drs Ferrari and Lentino, I removed the carcinoma of the esophagus following our modification of Torek's technique. Goyenechea administered spinal anesthesia with 20 centigrams of metycaïne, the patient being in supine lateral left position

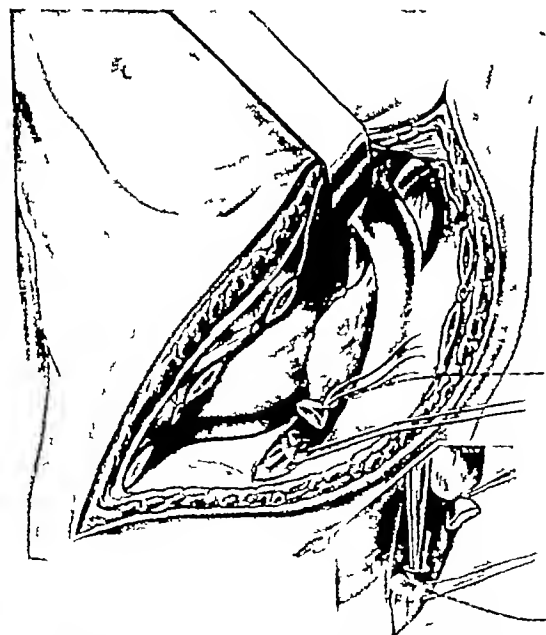


Fig 8 Division and ligation of the esophagus, above, and inset, invagination of the inferior stump beneath the pursestring suture made on the fundus of the stomach

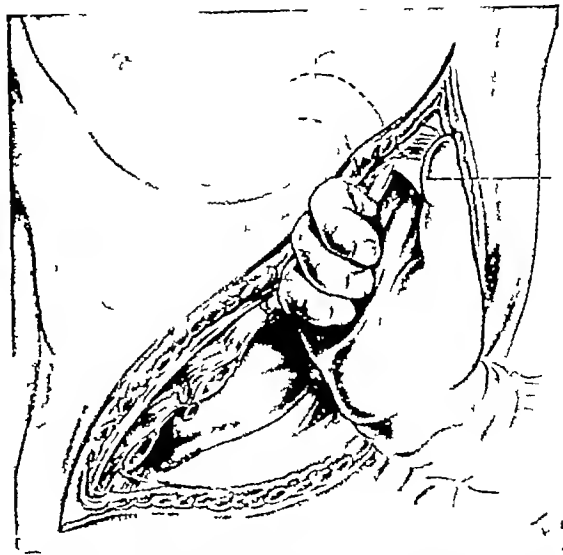


Fig 7 Freeing esophagus from aorta and from bronchus at level of which the tumor was located by digital dissection

Anesthesia was perfect throughout the entire thoracic stage of the operative procedure

TECHNIQUE

An incision is made the whole length of the seventh rib and is extended behind and above, following the interscapulovertebral space. The

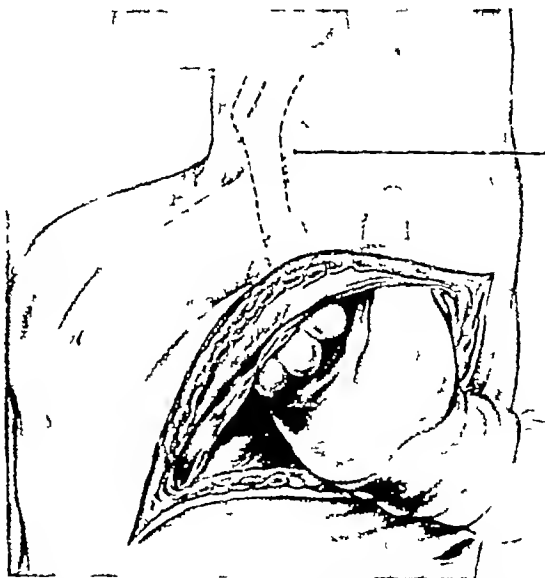


Fig 9 Dissection with the index finger extends to the cervical region above the isthmus of the thyroid gland (shown by dotted line)



Fig. 7. Exteriorization of the esophagus with the tumor, by simple traction. Removal of the tumor. Dotted line in inset indicates new position of esophageal stump.

incision includes the skin and cellular subcutaneous tissue. The wide muscles of the dorsum are divided down to the costal skeleton (Fig. 3). Careful hemostasis is maintained throughout the operative procedure.

The seventh rib is removed in almost its entire length, from the posterior angle to the neighborhood of its anterior end. About 8 centimeters of the sixth and fifth ribs are excised from the posterior angle forward (Fig. 4). The soft parts of the fifth and sixth intercostal spaces are excised between ligatures. The parietal pleura is opened in its entire length following the axis of the wound (Fig. 5). An Arce retractor is used to help to maintain the thoracotomy wide open. The lung is completely collapsed. A small quantity of serous fluid is usually present in the pleural cavity.

In front of the thoracic aorta, a few centimeters above the diaphragm, the mediastinal pleura is incised (Fig. 5). This incision is extended upward to the aortic arch. The esophagus is isolated by blunt dissection, and the tumor which has become a part of the esophagus itself is recognized (Fig. 6). In this case the tumor was attached to the bronchovascular arch. All the healthy

portion of the esophagus situated underneath the tumor is isolated from the cellular tissue of the mediastinum and the tumor is separated from its peripheral attachments by blunt dissection with the end of the index finger (Fig. 7). The esophagus is sectioned about 3 centimeters from the cardia after being crushed and doubly ligated. The inferior end is buried beneath a pursestring suture which is made by using the gastric wall. The superior end is protected with a piece of gauze (Fig. 8).

Dissection of the tumor is completed at the level of the bronchovascular region. Any fibrous attachments must be excised with scissors. Bleeding produced by this dissection is slight and is spontaneously controlled.

The mediastinal pleura is incised in the supra-aortic portion as the index finger lifts a fold of it. This incision is extended to the dome of the thorax. Digital dissection of the supra-aortic portion of the esophagus is carried out. The entire organ is then passed beneath the aortic arch and exteriorized through the incision in the mediastinal pleura.

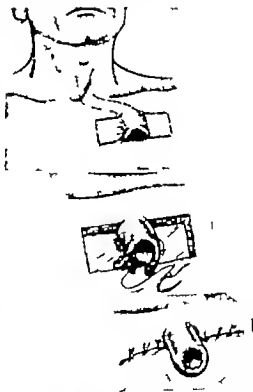


Fig. 8. Building of the "gargyle" to secure accommodation of esophagus and the latex rubber tube.

situated above it. The passing of the esophagus through the narrow passage situated underneath the arch is done by pulling its supra-aortic portion, and not its inferior tied end, and of course without folding it upon itself.

Once this passage is accomplished digital dissection is continued in all the upper portion of the thoracic and cervical esophagus (Fig 9). The index finger introduced through the supra-aortic incision of the mediastinal pleura makes this step in the operation very easy.

We would emphasize the fact that if the operator stands at the ventral side of the patient—a step not described previously—he is afforded better visualization of the esophagus thus facilitating dissection. Also, in this position it is always possible to use the right hand to free the esophagus from the thoracic walls.

The thorax is closed and the dissected esophagus is left with the tumor still inside (Fig 10). This closure is final. The mediastinal pleura is not sutured. The parietal pleura is sutured. The costal wound is approximated with two thick silk sutures. The muscles of the dorsum are closed with catgut. The subcutaneous cellular tissue is sutured. The skin is closed with interrupted silk sutures. While the wall is being closed, the anesthetist distends the lung progressively using



Fig 12 Photograph of the patient with apparatus in position



Fig 13 Roentgenogram of the thorax 5 months after operation. In the left side can be seen, below the clavicle, shadow of the "gargoyle" Metastasis is not evident.

high pressure in a closed circuit with the Foregger anesthetic apparatus, oxygen only being used, no anesthetic. The thorax is not fully closed until the lung can be seen completely distended, filling all the thoracic cavity. Then the thorax is closed without drainage.

The thoracic wound is covered with gauze, and the patient is placed in supine position with the head extended and turned to the right side. Local anesthesia is used. An incision is made following the anterior margin of the left sternocleidomastoid muscle. Incision includes the skin, subcutaneous cellular tissue, and cutaneous muscle. The sheath of the sternocleidomastoid muscle is opened at the level of its anterior margin. The muscle is pulled outward and the posterior leaf of the sheath is separated, thus revealing the cervical esophagus. This dissection is very easy because of the blunt dissection which already has been done via the thorax (Fig 10).

All of the thoracic esophagus is exteriorized through the cervical wound by traction in its cervical portion.

The esophagus is excised about 3 centimeters above the tumor. By blunt dissection a tunnel is built beneath the skin of the anterior aspect of the superior portion of the thorax. In the lower end of this tunnel which is almost vertical, a transverse incision 3 centimeters in length is made in the skin. The stump of the esophagus is intro-

duced through this tunnel and its terminal opening is sutured with silk to the cutaneous wound. The cervical wound is closed in two layers (Fig. 9).

During operation the patient remained in exceptional condition from both respiratory and circulatory standpoints. There was no dyspnea.

The mediastinal maneuvers produced some circulatory disturbance as evidenced by tachycardia and hypotension. Nevertheless the tachycardia did not last more than a few minutes. During the operation 500 cubic centimeters of physiological salt solution was injected intravenously.

At the end of the operation the circulatory condition of the patient was satisfactory. Pulse was 80, respiration 18, blood transfusion of 500 cubic centimeters was carried out.

After operation, the patient had rise in temperature from the first day, the temperature fluctuating between 37 and 38 degrees C. The pulse stayed between 80 and 90. Routine therapeutic measures were carried out, saline and glucose solutions were administered, cortical suprarenal extract as given in large doses. A fairly normal diet was maintained by means of the gastrostomy.

On November 4, 6 days after the operation, pleural collection was evident and as confirmed by the x-ray picture. A small thoracotomy was performed through an intercostal space to introduce a French catheter No. 20 and 750 cubic centimeters of serosanguinolent fluid was drained. Drainage was maintained. Examination of the fluid obtained showed the following: few streptococci and Gram positive diplococci were observed, normal quantity of degenerated leucocytes and abundant normal erythrocytes were also observed.

The temperature continued to fluctuate between 37 and 38 degrees for some days more with corresponding variation in pulse. Any movement caused tachycardia which however improved little by little. Outside of these abnormal periods the pulse stayed between 80 and 90. Under these circumstances Dr. Marcelino Cane-

pane, who had been of great help during the postoperative period, advised the use of antiseptics. This therapeutic measure was very effective.

The wounds of the esophagostomy and of the thoracotomy healed *per primam*. Because the suture lines continued to function through the esophagostomy irritated the skin and a secure better means of feeding the patient, on November 11, connection was established by means of a rubber tube between the upper stump of the esophagus and the gastrostomy opening. The tube worked well and the patient was able to eat in the normal way.

The rubber connection functioned well for period of more than 10 days, it served not only to feed the patient but also to direct the suture lines toward the stomach thus preventing it from going through the esophagostomy. Little by little, however, the esophagus became ulcerated with about the clavicle, and subsequent cervical cellulitis was produced. Once the tube was withdrawn the cellulitis improved, but in the suprascapular region a small epipharyngeal fistula persisted that did not tend to heal. It then used suction pump to effect continuous suction of the suture. The fistula closed in a few days and the skin returned to normal condition.

A pleural suppuration, caused by the silk threads which approximated the ribs, made necessary the removal of the sutures under local anesthesia.

At present, 3 months after the operation, the patient is well. He gained 3 pounds in weight and nutrition is good. The red and white blood cells are again normal.

To secure more perfect fitting between the esophagus and the India rubber tube, on January 30, 1931, removed the esophagus with silk. Then, formed sort of a gurgyle which is introduced in the India rubber tube (Fig. 10 and 11). The feeding of the patient is satisfactory. It has not yet been decided to build prethoracic esophagus. It is intended to do this once the usual period of recurrence has passed.

(Complete bibliography is to be published in later issue of *Boletín del Instituto de Clásicos (Mérida)*.)

(Translated by Miss F. R. Sells, secretary Institute of Surgery Buenos Aires.)

LUNG INJURY DUE TO THE DETONATION OF HIGH EXPLOSIVE

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Columbus, Ohio

TO the neutral observer this war is truly different from previous struggles, different in its conception of attack and defense, as well as in the vulnerability of the civilian population. As a result of the development of the bombing attack, attention has been directed to new problems of war injury. Numerous reports have appeared concerning the effects of detonation of high explosive. And attention has been called to the fact that many deaths occur without evident gross injury to the body, while the necropsy reveals varying degrees of trauma to the lung. Many clinical and experimental studies have been made on the differing types of injury due to "blast" and the results appear to have given rise to varying conclusions. Moreover, in recent discussion appearing in the American literature little or no attention has been directed to this form of lung injury. It is, therefore, the purpose of this paper to review critically the recent clinical and experimental studies that have been made on the effects of detonation of high explosive, particularly on the pulmonary system, and to compare them so far as possible with the "similar" forms of lung injury as observed in peacetime civilian life.

PEACETIME INJURIES OF THE LUNG

Lung injury in the intact thorax, apart from a few isolated cases, has received but little mention in the English surgical literature. Its occurrence was recognized and described as early as 1761, when Morgagni reported two postmortem findings. Richter, in 1904, and Schwartz and Dreyfus in 1907, each gave a good account and a review of the current literature, and Fischer wrote an excellent monograph in 1912.

Thoracic injuries are to a certain extent comparable with those of the abdomen and skull in that attention is devoted less to the parietal lesion than to the possibilities and extent of damage to the contained viscera (Smith, 1840,

From the Department of Research Surgery of The Ohio State University. Dr. King, Comby Fellow in Research Surgery, served as surgeon to the First Base Hospital for the Chinese Army at Shanghai during its repeated bombing and eventual capture by the Japanese in 1937 (G.M.C.).

Sellers, 1933). Many of the cases reported were the result of severe crushing violence to the chest and the diagnosis was not usually made until postmortem examination.

Physiological anatomy of the thorax. Most writers are agreed that injury to the thoracic viscera is more frequent in children and adolescents and that this is resultant to the elastic nature of the juvenile thoracic cage. It has been suggested that the lung is simply compressed between the more resilient ribs or against the vertebral column.

In a series of experiments on the thorax after removal of the contained viscera, Triepel (1902) made the interesting observation that the male thorax can withstand more lateral and the female more sagittal pressure. Kulbs (1909), in his animal experiments, found that the chest yields more to a blow from the front and, as a whole, is less capable of resistance to this injury. Compression of the thoracic cage, according to Limon and Pera (1921) causes immediate diminution in its size, primarily at the expense of the mobility of the costovertebral and costosternal joints. When the motility of these joints is insufficient, a new factor intervenes which is determined by the elastic properties of the costocartilaginous cage.

The presence of air within the lung at the time of injury was discussed by Gosselin (1845), Gross (1866), LeConte (1908) and Adams (1933). It was pointed out that sudden compression of the air within the lung causes the lung to rupture owing to the resultant instinctive closure of the glottis, together with the withholding of breathing, thus making it impossible for the pulmonary sponge to empty.

Peyrot (1907) stresses the anatomicophysiological arrangement of the pleura. The normal cohesion of the pleural surfaces holds the lung to the parietes. Thus, if the chest wall with its parietal pleura and the lung with its visceral pleura are depressed, the remainder of the lung is prevented by its natural adherence to the chest wall from following the movement. A part of the organ which is seldom stretched is thereby put under tension and tears may result.

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Fig. Gross appearance of the lung after injury by contusion in peacetime civilian life. Note the scattered areas of hemorrhage.

Du Séjour (1901) agrees that the mechanism stressed by Peyrot would explain rupture if the pleura were adherent, but thinks otherwise that there is too much gliding between the pleural surfaces. In his opinion the air-filled lung is abruptly compressed at the time of trauma and escape of the air through the upper air passage is insufficient. Hence rupture results by sudden compression as one might burst an inflated paper bag. Similar opinion was expressed by Gross (1866).

Joannides and Tsoulos (1930) after experimental work on the production of mediastinal emphysema in dogs, came to the conclusion that anything which produces an increased intrapulmonary pressure such as a severe cough, the labor of childbirth, lifting of a heavy weight, etc., probably causes a mild degree of mediastinal emphysema and air embolism, which as yet we have no way of recognizing clinically.

Morbid anatomy for injuries. The morbid anatomy of the injuries varies greatly. In simple

contusion, bleeding occurs into the lung substance as Duval (1918) has shown, producing areas of contusion at the base and apex of the injured lung with blood infiltration of varying extent—simple contusion by *contre-coup*. Duval even demonstrated small tears of the visceral pleura on the opposite side.

Rupture of the alveoli with interstitial emphysema about the capillary vessels was also noted recently in the animal experiments of Adams (1933) carried out by simulating a submarine escape. Sometimes the hemorrhage is severe and may be localized to one lobe as in an instance reported by Sauerbruch (1937). It can be even more marked as in the case of Rocher and Dupérol (1927) which is typical of gross hemorrhagic infiltration of both lungs without apparent tears in the pleura. Similar observations were also reported by Duval.

Flacher (1912) gave an anatomical classification of rupture of the lung according to the severity and site of the lesion: (1) Crushing into a shapeless mass of one lobe of the lung or of the whole lung; (2) internal rupture of the lung with intact visceral pleura; (3) complete penetrating rupture of the lung; (4) separation of one lobe of the lung.

Cooke (1936) more recently presented a clinical classification of pulmonary injuries: (1) the pneumothorax type; (2) parenchymal rupture—this is a simple rupture without laceration of the visceral pleura; (3) combined types.

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Lung injury without trauma to the thoracic cage may be produced by the following causes: (1) Run over by a heavy vehicle—accounts for 2 out of 70 cases in Flacher's series—W. Ison, Smith, Tatum, Johnson, Harlan, McDonnell, Ashburn, Laurent, Kerr, Meroude, Richter, LeCoute, Ville gas, Sauerbruch; (2) blow on the chest—Davies, Bogdan, Spiers, P. J. Scott, Connolly, Dieffenbach, Head, Fallon; (3) fall from a height—Gosselin, Gross, Wharry, McTaggart; (4) lifting a child by the arms—Cockle; (5) glancing blow of a bullet—Rees; (6) increase in the intrapulmonary pressure by coughing—Stranek, Sauerbruch, during parturition—Cunnington, dyspnea during tracheotomy—Werwath, violent respiratory effort—Waters; (7) nearby explosion—Delacroix, Ravaut, Thomas, Sencert.

ILLUSTRATIVE CASE REPORT

An example of this type of injury from our own records is presented as follows:

Autopsy No 1238-1581 (Arch 1097) White boy, aged 12 years. The history relates that he was playing with two other boys at the city gravel pit. They built a cave in the side of some loose shale. The roof suddenly caved in and the boy sustained a heavy crushing blow on the chest by large pieces of falling shale and loose earth. When dug out he was found bleeding from the nose and was brought immediately to the hospital. He was pronounced dead upon reaching the hospital.

On examination blood was found in the ears, nose, and mouth. No other abnormality was found. The clinical diagnosis was fracture of the skull.

Postmortem examination revealed fracture of the base of the skull. The left lung weighed 350 grams. The pleura was unusually hemorrhagic. The lung was expanded and many small hemorrhagic spots appeared scattered over its pleural surface. On its cut surface appeared numerous areas of petechial hemorrhage. The bronchi were filled with foamy blood. The right lung presented identical changes (Fig 1).

Microscopic examination of the lungs revealed multiple areas of hemorrhage of varying size scattered throughout the entire lung. Many of the alveoli appeared disrupted and filled with red blood cells. The bronchi and bronchioles were also filled with red blood cells (Fig 2).

This is an instance of peacetime injury of the lung without evidence of external injury. It was not recognized clinically. The fact that extensive visceral damage can be produced without revealing any *external* evidence is important from many points of view. The clinical significance of this example is obvious and has been recognized by certain surgeons.

THE NATURE OF HIGH EXPLOSIVE EFFECTS

Having reviewed traumatic lung injuries without external lesion as they are encountered in peacetime civilian life, it remains to compare them with the lesions produced by the detonation of high explosive. Many have a vague knowledge of the nature of explosives. This doubtless explains their ready acceptance of fantastic stories of the discovery of explosives of extraordinary power, tales of which are so often circulated.

"Explosion" has been defined as "the act of exploding, a rapid combustion, decomposition or similar process resulting in a great and sudden development of gases, and consequent violent increase of pressure, usually causing a loud report."

"Explosive" is any substance that may cause an explosion by sudden combustion or decomposition. Two categories are recognized, low and high explosives. Low explosives are those having explosion velocities of a few thousand feet per second or less. Members of this group are characterized by a comparatively slow "push" type of explosive effect. High explosives are those having explosion velocities of from 5,000 to 25,000 feet per second and, consequently, have quite a different effect. The violence of their detonation produces an

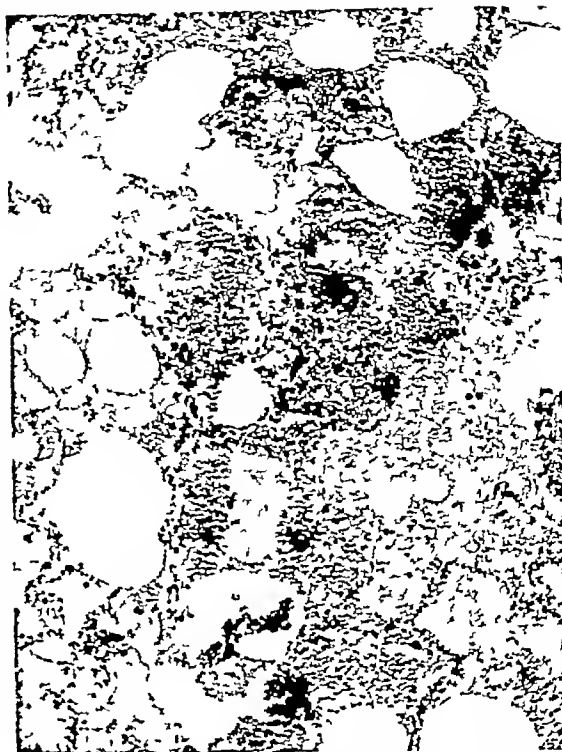


Fig 2 Photomicrograph of the lung appearing in Figure 1. Note the hemorrhagic exudate in the ruptured alveolar spaces.

extreme shattering effect in the immediate vicinity.

"Detonation" is a violent explosion, one resulting from practically instantaneous decomposition or combustion of unstable compounds.

A "bomb" has been defined as "a hollow projectile of iron, generally spherical, containing an explosive material which is fired by concussion or by a time fuse, also any similar receptacle of any shape containing an explosive, as a dynamite bomb" (Muehlberger, 1937).

The British speak and write of the immediate effect of the detonation of a modern high explosive bomb as "blast."

The chemistry of high explosive High explosives depend for their action upon the instability of the chemical equilibrium of their constituents. They consist of compounds of carbon, oxygen, nitrogen and hydrogen so feebly combined that when fired by combustion or detonation, new, simpler and more stable gaseous compounds are formed. Once chemical action is started it proceeds with great velocity and the explosive is immediately converted into gases with the evolution of heat. These

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gases, now occupying an enormously greater volume than the original substance have powerful disintegrating properties. High explosives are violent detonating at the rate of several miles per second, many times greater than the speed of the most violent hurricane (Bloam, 1882 Logan 939 Storm 939).

The nature of Blast. By blast or explosion is further designated the compression and subsequent suction wave which is set up by the detonation of high explosive. At every point in the immediate neighborhood there occurs first a momentary wave of high pressure (for about 0.006 seconds for a 70 pound charge) and then a negative suction pressure due to the fact that the positive compression wave has reduced the density of the air behind it to below normal atmospheric pressure. Like the pressure component, the suction component of the blast wave lasts but for a fraction of a second, yet as a rule for a longer period than the compression wave (p to 0.3 seconds for 70 pound charge).

The wave of pressure is highest in the immediate region of the explosion and falls off rapidly as it moves away. Thus 15 feet from a 25 pound charge, the hydrostatic pressure may be of the order of 200 pounds per square inch, whereas 50 feet away the maximum pressure recorded will not be more than 10 pounds. Everything in the immediate neighborhood of the explosion of a big bomb will therefore be suddenly exposed to a violent pressure wave of many times atmospheric pressure, whereas everything 50 feet away will be exposed to only two or three atmospheres of pressure.

The suction component of the blast wave is always weaker than the pressure component and in no case can it be greater than 15 pounds per square inch since this corresponds to complete vacuum. The magnitude of the pressure and suction components of a blast wave are correlated directly with the amount of explosive and are much higher for larger than for smaller amounts (Rochmary 1910 Taylor 932 Zukerman 1940).

The physics of blast. The prime characteristic of any form of wave motion is that whereas the disturbance itself moves forward, the particles of the medium through which it passes do not move with it, but oscillate backward and forward about the position of equilibrium. The plane of oscillation may either cross the line of propagation, called transverse waves, or parallel the line of propagation called longitudinal waves.

For the sake of simplicity imagine that the origin of the blast is a small sphere of explosive material. When this is detonated it expands suddenly

and compresses a spherical shell of air immediately surrounding. Thus the blast wave consists of a compression followed by a rarefaction as it is propagated outward.

The maximum movement of any air particle on each side of its normal undisturbed position is called the amplitude of the wave and clearly depends upon the violence of the explosion. In the case of aerial bomb explosions such as are now being experienced in Europe, the amplitudes are considerable for in the compression part of the wave pressure up to 200 atmospheres—that is, and 35 tons per square inch—have been observed.

The phrase "beating the air" is commonly used to denote ineffectiveness. Beating the air is normally ineffective because the mobility of the air generally makes it easy for it to escape around the edges of the vulnerable object. The more sudden and violent the beating the less is this true, and the more will the air act not like a mobile gas but a rigid object, so that the violence of blast can even bruise the walls of the lung as if they had been hit by a solid object (Bertelot, 1885 Barlet, 1931 Sutherland, 1940).

THE EFFECTS OF DETONATION OF HIGH EXPLOSIVES

The extraordinarily varied effects of bombing on buildings in cities and towns have been vividly described and minutely detailed by Flakine (1938) Langdon-Davies (1939) and others from their experiences in the Spanish War. They described how when bombs burst in a street, the metal shutters of the shops which had not been hit were socked outward. When a bomb exploded inside a house, large part of the shattered walls fell inward.

According to Logan (1939) Zukerman (1940) and others, a man may be wounded by a bomb explosion either by being hit by fragments of the bomb-casing or by masonry or some other hard substance falling or sent flying by the explosion or by being violently thrown or by being affected by the blast wave without being thrown.

Lockwood (1940) and Logan reported that during World War I (1914-1918) men were sometimes picked up in the field dead from an explosion without revealing any external injury and some times with blood-stained fluid trickling from the nose or mouth. Similar experiences were described by Mogina (1938) Langdon-Davies (1939) and Mitchener and Cowell (1939) in the Spanish War.

Again, in this war there have been reports of the damaging effects of blast on domestic animals. The damage to the lungs, characterized by al-

veolar rupture and hemorrhage, has been the consistent and dominant feature

CLINICAL INVESTIGATION

Early observations The literature on this subject is limited because this form of injury was not well known prior to the last war (1914-1918). Nevertheless, the earlier clinical observations had led to the belief that the lesions and death from the explosive effect were due either to gases such as carbon monoxide produced from the detonation of the explosive (Brouardel, 1887, Cenas, 1887, Dujol, 1887, Servel, 1887, Mitchell, 1897, Urie, 1904, Bahier, 1905, Fabre, 1906, Hatton, 1911), or resultant to a sudden vacuum effect in those parts of the body which contain gas, e g the lung lobules, stomach, or intestine. Thus, experimentally, gas bubbles may be set free in the blood by the sudden evacuation of a chamber in which an animal is placed. These bubbles may then block the circulation as in compressed air workers or deep sea divers when they are too rapidly decompressed (Bert, 1875, Granjon-Rozet, 1877, Gaudin, 1887, Guinand, 1887, Reynaud, 1887, Thomas, 1917, Hill, 1917).

The earlier clinical observers also reported that this form of trauma produces injuries in the nervous system (Hinchliff, 1875, Coskery, 1877, Duret, 1877, Michel, 1878, Tryon, 1891, Matignon, 1907, Zangger, 1907, Querleux, 1908, Etonensis, 1909, Llewellyn, 1910, Sterlin, 1912, Claude, 1914, Laurés, 1915) and in the lung (Reynaud, 1887, Paucot, 1901, Delacroix, 1907, Ravaut, 1915, Thomas, 1915, and Sencert, 1915).

Recent observations Gatti (1918) presents a case of acute paralysis with subsequent atrophy following the explosion of a large bomb without actual contact. The condition was similar to that seen in anterior poliomyelitis and the assumption is made that the concussion injured the motor portion of the spinal cord. Similarly Cramer (1919) reports the case of a young soldier who presented the signs of a severe aortic insufficiency after being thrown several feet into the air by the explosion of a bomb. This patient had previously been healthy and had not had those diseases which might predispose to such a heart lesion.

Mott (1916, 1917) reported several patients as having died of explosive concussions in which two outstanding lesions were observed. First, the hematomas present in the lung, and second, the extreme vascular injury to the brain. He believed that the enormous aerial compression "may be transmitted to the fluid about the base of the brain and cause shock to the vital centers of the floor of the fourth ventricle, causing instantaneous

arrest of the function of the cardiac and respiratory centers." This, he held, explained many of the instances of sudden death in which no visible injuries to the body were evident. Similarly Haldane, in describing a personal experience of his own during World War I when he was in the vicinity of bursting shells, thought that death under such conditions might be due to respiratory paralysis. Other similar observations of injury to the nervous system from the effect of explosion were also reported by Chavigny (1916), McWalter (1916), D'Abuno (1916), Meige (1916), Littermitte (1917), Pachanton (1917), and Marage (1918).

Mogena (1938) saw several instances of soldiers in Spain suffering from violent "bodily commotion" from proximity to a bursting shell. Examination of those killed by explosion (without obvious external injury) may reveal a tear of the lung, or a bulbar hemorrhage in others who live for a time, rupture of meningeal vessels, hemorrhage from intestinal laceration and other internal trauma. In some the hemorrhage might not appear for 2 to 3 days. The author explains this as due, in his opinion, to gas embolism from sudden atmospheric decompression.

Falla (1940) reported a case with capillary hemorrhage in both lungs due to blast. The patient died 12 hours following operative intervention for bleeding from a laceration of the thigh after the use of open ether anesthesia (Fig 3).

Dean and Allison (1940) observed 27 instances, and in all but two evidence of serious or gross pathological changes in the chest was absent. They called attention to the relative disproportion in frequency between the symptoms and physical signs in the cases studied, the frequency of a ballooned appearance of the chest and the radiological appearance of a diminution of rib expansion. A similar observation was made by Rose (1940).

Roberts (1940) pointed out the contraindication to surgical operation. Of two patients whose abdomens had been opened for intense abdominal symptoms, neither presented any demonstrable lesion and the thoracic injury appeared to be the real cause. He calls attention to the fact that if a group of bomb casualties contains one blast case it probably also contains others, even though the signs and symptoms are lacking.

Hadfield et al (1940) reported 10 cases of sudden death in persons subject to the blast effect of high explosive bombs. In none of these was there any evidence of external trauma. There were gross hemorrhagic lesions in both lungs in all, and blood stained secretions in the upper air passages in



Fig. 3. Photomicrograph of the lung of a man who died as a result of injury sustained in an air raid (Fallin's case). The alveoli, which are disrupted, are filled with blood cells. (After Zakarian.)

some. Again they reported a case in which a man aged 23 lived for 51 hours after exposure to a blast. As a result of this observation they believe that patients who develop pulmonary hemorrhage without external trauma to the thoracic wall continue to bleed into the lung for a period which may amount even to 48 hours. In the light of the post mortem finding of continued bleeding they concluded that these patients should be treated as strictly as if they had had recent severe hemoptysis (Fig. 4).

O'Reilly (1941) stated that from 3 cases which he had studied one clinical point had emerged that within 48 hours in 2 and within 4 days in the other the clinical findings of an ordinary lobar pneumonia had apparently developed. Again 5 patients belonging to the same "incident" were brought in with the appearance of acute abdominal catastrophe—rigid abdomen, pain, and so on. Two were sufficiently serious to require surgical intervention, but nothing was found except a few minute subserous hemorrhages.

Ross (1941) made a comparative postmortem study of peacetime and wartime lung injuries and concluded that the main points of difference may be summarized as follows:

In compression asphyxia the lesions may be symmetrical on both sides but not necessarily. The hemorrhages are usually subpleural and in the

lines of the ribs. There is generalized pulmonary congestion.

2. In hemorrhage due to impact of a solid the hemorrhage is in relation to the point of maximum impact and may be unilateral. The lung tissue is contused, torn and filled with blood at or around this point.

3. In "hemorrhagic concussion" (due to blast) the lesions are always bilateral and roughly symmetrical. There is general congestion of the lung. Pleural hemorrhages are present only as an extension from deeper areas.

Osborn (1941) from the results of his comparative study of peace and wartime injuries to the lungs states that there are two forces which bring about the capillary hemorrhage in hemorrhagic concussion. These are compression of the lungs through the chest wall and diaphragm and the counterpressure exerted by the air in the alveoli. The actual lesion is mainly hemorrhagic from the alveolar capillaries. The lesion itself is not progressive as Hadfield et al. claim, but the reaction is. Treatment is largely in the anticipation of complications.

In conclusion he states that to understand the lesions described for blast in animals and men there is no need to assume that blast has any mysterious properties. It is only a more severe diffuse sudden compression of the chest and abdomen than we see in civil cases during peacetime.

Robb-Smith (1941) after the study of 789 consecutive accident cases of all types again called attention to the fact that the pulmonary symptoms which arise from exposure to the blast of high explosive may be due to a combination of pulmonary concussion and fat embolism, and fat emboli should be specifically looked for in autopsies on air raid casualties. A similar observation was also reported by McKillop (1940) from his experimental study.

Experimental observations. The prevailing idea formerly was that the nervous system was especially sensitive to this form of trauma. This received the support of Mott and others. However clinical and postmortem observations have now established that the pulmonary lesions predominate.

Carver and Dinley (1919) report experiments on fish, rats, and mice. They state that the animals which were more exposed to detonation showed hemorrhages from the ears, nose, and mouth and when sacrificed exhibited varying degrees of internal hemorrhage in the viscera and central nervous system while the alveoli of the lungs were nearly always found to a certain extent ruptured.

Mairet and Durante (1919) have published several reports concerning concussion shock, the last of which presents their conclusions and opinions based upon a considerable amount of experimental work. They exposed rabbits to the detonation of high explosive under various conditions and made a particular study of the resultant lesions. The symptomatic behavior of the animals was also noted. The viscera of the animals at necropsy were found to be normal except for the lungs which were spotted with hemorrhagic areas. On the surface of the cord in all cases they found varying amounts of blood suffusion, irregularly distributed, with small clots adhering to the nerve roots. The brain appeared normal or showed petechial hemorrhages at various points on the surface. Upon these observations they developed a theory that concussion shock is due to vibrations set up in the atmosphere which, transmitted to the organism, act injuriously by violently agitating the unprotected tissues.

Hooker (1923) determined the physiological effect of air concussion. Experimental observations were made upon dogs, cats, rabbits, and frogs exposed at various distances to small charges of explosive and to gun-blast. According to this investigator, bruising with rupture of the lungs was the single gross lesion found postmortem, and this lesion was probably the primary cause of death when it occurred.

Barcroft (1940) also investigated the physiological effects of "blast" and established four points from his experiments: (1) that only animals placed in the open and within 15 feet from the exploding bomb suffered ill effects, (2) that the Anderson shelter gave immunity at 15 feet and outward to "blast" injuries, (3) that the animals situated further than 15 feet suffered no demonstrable lesion of their organs, and (4) that the lesions found in the animals nearest to the explosion were essentially in the lungs. Histologically, these lesions consisted of bruising of the lung surface along the line of the ribs and vertebral borders, and extended for one-quarter to one-half inch into the lung tissue. Other small hemorrhages were found deeper, especially around the small bronchi. From a study of animals observed over a subsequent period of weeks, the exposure to "blast" appeared to have had no permanent effect.

Until recently, the manner in which the pulmonary lesions are caused by the "blast" had not been studied. Various workers have, however, speculated about this on the basis of the character of the lesions and three possibilities have been suggested. The first is that the lesions are due to



Fig. 4. Cut surface of the lung of a girl found dead in a public shelter which received a direct hit by an aerial bomb. Note the distribution of the hemorrhages which are most extensive in the deeper parts. (After Hadfield et al.)

the lowering of alveolar pressure by the suction wave, acting through the respiratory passage with the consequent rupture of the alveolar capillaries. The second is that the lesions are caused by the distention of the lungs with air. The third is that the lung lesions are due to the impact of the pressure wave on the chest wall.

Zukerman (1940) in a recent, more elaborate investigation designed to determine the mechanism by which the lung lesions were produced, confirmed the extensive injury to the lung tissue in a wide variety of animal species. The view which his experiments substantiated was that the lesions were due to the impact on the thoracic wall of the pressure component of the blast wave. Rabbits were exposed to the explosion of hydrogen and oxygen in balloons. When very close to the bal-



Fig. 5. Moderately severe hemorrhages in the lungs of rabbit exposed to blast. (After Zukerman.)

loon the lesions were found mainly or entirely localized on the side facing the balloon. It appeared to be a direct impact effect and not some more general pressure effect through the trachea. In the latter instance the lesion would be expected to be bilateral. In another set of experiments one half of the animal was covered with sponge rubber. If the covered side were placed toward the explosion the animal sustained practically no lesions, but if the covered side were away from the explosion it received many lesions on the uncovered side facing the explosion.

Near the explosion of a 70 pound charge (at 13 to 18 foot distance) the animals would be found dead within one minute. At these distances the positive component of the blast wave (hydrostatic pressure) varied between 120 and 63 pounds per square inch. Further away in a zone of lower pressure (at 8 to 20 feet) the animals would die as a rule within 24 hours. The clinical features were fairly constant including air hunger and dyspnea. Still further away was one (at 30 to 50 feet) in which the animals survived and recovered and in which they showed no external appearance of injury though postmortem examination revealed characteristic visceral changes.

In none of the animals which died was there any external sign of injury and in no case were fractures observed. The predominant lesion was bilateral traumatic hemorrhage in both lungs vary-

ing in degree according to the distance of the animals from the explosion (Fig. 5).

Microscopically the lesser degrees of damage appear as a small zone in which the alveoli and the smallest bronchioles are filled with blood. The alveolar walls are often disrupted the hemorrhage originating in the torn alveolar capillaries. In severe grades of damage large areas of the lung are disrupted and hemorrhagic and the larger bronchi become filled with blood (Fig. 6).

No changes were observed in the other organs and tissues of the body. Zukerman concluded by emphasizing that in the case of fatal injuries due to blast, what actually caused death in such cases—in fact, what caused death in experimental animals subjected to blast alone was not known, and it was to the solution of that problem that some experiments at the present are being directed.

Stewart et al. (1941) more recently report their experimental investigation of blast injury to the central nervous system. Again, they emphasize that lesions of the central nervous system may be produced. They state that though pulmonary damage is apparently a constant finding and at times is very extensive it seems unlikely that it is responsible for either sudden death or later fatalities except in a contributory way. They suggest that the mechanism responsible for the cerebral lesion was the hydraulic like pressure on the central nervous system, in its firm encasement, resulting from sudden compression of the thoracic cage with consequent violent back-pressure on the venous side.

TREATMENT OF THE INJURED

Prevention. On the basis of both the clinical and experimental observations it may be stated that prophylaxis is possible. And there are two measures of direct importance in the prevention of this form of trauma.

First is the application of the general principle of protection from the blast wave by the use of air raid shelters and the like such as ditches, holes, and gutters on the ground. As an emergency measure one should lie flat on the ground in the prone position, since the back yields less to injury than the front part of the chest.

Second is the application of some direct measure of protection by covering the chest with sponge rubber or some similar material.

Management after the injury. The importance of early recognition of the lung injury in order to treat it rationally cannot be overemphasized. If, for example, as the result of careful clinical observation it is concluded that pulmonary lesions are

present in those whose degree of shock is out of proportion to the apparent severity of the injury, then the indication will be to avoid unnecessary operative intervention and open anesthesia and to concentrate on the treatment of the shock.

It is too soon to determine in full the treatment which may be required. *Complete rest* is essential, and in view of the condition of the lungs found at necropsy and the embarrassed breathing clinically, every effort should be made to avoid any additional trauma and work that might be added to the already traumatized lungs. Oxygen therapy would consequently appear to be worthy of more extensive use. Above all, an awareness that such damage to the lungs may occur should stimulate all concerned to be watchful for this hidden type of danger among those injured in air raid casualties.

SUMMARY

This war differs from those preceding in that aerial bombing has assumed a dominant rôle in the attack. Consequently, the civilian population is, at least in certain phases of the struggle, more vulnerable to attack than the military personnel. This new technique of warfare has created other problems of injury and particularly to the lungs, however, lung injury in the intact thorax occurs more frequently during peacetime than has been formerly recognized and reported.

The pertinent physiological and morbid anatomy of the thorax is reviewed. A case of lung injury unrecognized clinically and discovered at postmortem, similar to that of the lung injury from blast is presented. A brief review of the power of high explosive, and of the nature and physics of the explosion is presented. The outstanding clinical findings of blast injury to the lungs are as follows:

Symptoms may vary from a slight degree of respiratory distress to a complete cessation of respiration depending on the degree of injury inflicted by the blast wave. In general, varying degrees of shock are present accompanied by dyspnea. Cough and hemoptysis also are frequent. Symptoms referable to abdominal and cerebrospinal nervous disturbances have been reported.

Physical examination reveals, in general, no gross injury particularly pointing to the thorax. However, one clinical aspect of importance dealing with this type of injury that demands constant attention is that the gross lesions found elsewhere in the body must not be allowed to overshadow the possible lung injury which is now known to be probable without evidence of external



Fig 6 Photomicrograph of the lungs of a rabbit exposed to blast, showing many alveoli filled with blood cells and the disrupted alveolar walls (After Zukerman)

injury to the chest. The importance of this special precaution, clinically, cannot be overemphasized. The presence of blood in the nose or mouth and bloody sputum, and the characteristic x-ray appearance of the chest are of considerable diagnostic importance.

The *postmortem findings* always reveal extensive hemorrhagic lesions in the lungs. All cases show general pulmonary congestion. Pleural hemorrhages are present only as an extension from deeper areas.

The results of the experimental studies carried out by various investigators have confirmed the clinical and *postmortem* findings that pulmonary lesions predominate. The view substantiated by the recent experiments is that the lesions are due to the impact on the thoracic wall of the pressure component of the blast wave. More recent studies have again called attention to the evidence that lesions of the central nervous system may be produced by blast. It has been suggested that the mechanism which is responsible for the cerebral lesion was the hydraulic-like pressure developed from sudden compression of the thoracic cage with consequent violent back pressure on the venous side.

Prevention of this form of injury is better than treatment. Both the general and direct measures for prevention have been discussed. The principles of treatment have been discussed in the light

of the available clinical and experimental observations and attention is called to the necessity of keeping in mind this type of lung injury regardless of whether injuries are found elsewhere in the body.

CONCLUSIONS

1. Lung injury without external evidence of trauma occurs more frequently in peacetime than has been recognized and reported.

2. In a bomb explosion the pressure wave of the blast may produce pulmonary lesions without resultant evidence of injury to the thoracic cage. The lesions are principally due to the impact on the body wall of the pressure component of the blast wave. That this form of trauma produces lesions predominantly in the lung is now abundantly confirmed.

3. It appears that the mechanism responsible for the cerebral lesion is the hydraulic pressure on the central nervous system, in its firm encasement resulting from sudden compression of the thoracic cage with consequent violent back pressure on the venous side and that this mechanism may prove

to be the explanation for the cause of sudden death in certain cases reported.

4. Prevention is better than treatment; the necessity of providing adequate general and direct protection, particularly to those who are prone to exposure to the bombing attack is evident.

5. After injury complete rest is essential. Every effort should be made to avoid any additional trauma and add extra work to the already damaged lungs. Oxygen therapy should be used more extensively.

6. The knowledge that such damage to the lungs may occur should stimulate all to be watchful for this type of injury especially among our raid casualties.

7. This review by no means concludes the problem of lung injury due to the detonation of high explosives. It is hoped that present and future investigations will bring greater and more accurate knowledge.

(A complete bibliography will be contained in the reprint of this article.)

CAUDAL ANESTHESIA

Its Use in Obstetrics

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FOLLOWING the successful use of caudal anesthesia in proctological operative procedures at the Milwaukee County General Hospital, its adaptability to the obstetrical service was tested. A brief review of the first 400 cases of series in which it was tried is presented.

HISTORY

In 1895, Corning first suggested the possibility of introducing an anesthetic solution into the epidural space. In 1905, Cathelin, a French urologist, blocked the sacral and coccygeal nerves through the sacral hiatus (22). Four years later, Stoeckel used caudal anesthesia with some success in obstetrics. His technique was improved upon by Laewen and Schlimpert, in Germany in 1910. In America, Meeker and Bonar used it successfully in gynecology, in 1923, others followed Oldham in 1925, Lundy in 1928, Henry and Jaur in 1929, Rucker in 1930, Campbell in 1935, Johnson in 1936, Sword in 1936, and Baptista in 1939.

DEFINITION

Caudal block, also known as extradural or epidural block, as defined by Labat, consists in passing a needle through the sacral hiatus and depositing an anesthetic fluid within the sacral canal. The solution is distributed outside of the dura mater and the process is thus differentiated from spinal anesthesia, in which the anesthetic is introduced into the subarachnoid space.

Caudal block is not to be confused with transsacral block, obtained by anesthetizing the sacral nerves through the four posterior sacral foramina, which represent the spaces between the fused sacral vertebrae. Presacral or parasacral block, on the other hand, is the procedure by which needles are passed through the perineum, anesthetizing the sacral nerves at the points of their exit from the inferior sacral foramina by the deposition of the agent into the hollow anterior aspect of the sacrum. A combination of caudal block plus transsacral block is designated as sacral anesthesia.

ANATOMY

Throughout the length of the sacrum, the vertebral or spinal canal is continuous as a prismatic space, 6 to 8 centimeters in length, known as the sacral canal. Following the curvature of the sacrum, its anterior and posterior walls are formed by the fusion of the bodies of the vertebrae, and are perforated by the anterior and posterior sacral foramina, through which the sacral nerves course outward. The dural sac, ordinarily terminating at the level of the second sacral vertebra, constitutes the upper boundary of the sacral canal. The lower end of the sacral canal tapers down to the sacral hiatus, an aperture on the posterior surface of the sacrum, usually comparable in size to an adult's thumbnail. This hiatus, due to the embryological failure of development of the spinous process and the laminae of the fifth sacral vertebra, is usually triangular in shape, the apex being designated by the fourth sacral spinous process while the base is bounded laterally by the sacral cornua, bony projections which articulate with the corresponding coccygeal cornua. Not infrequently the hiatus is found to be diamond-shaped rather than triangular. This impression is received when a tubercle, the rudimentary spinous process of the first coccyx, is prominent in the midline and forms the lower angle of the rhomboid. The sacral hiatus is covered by a fibrous membrane, the sacrococcygeal membrane of Cathelin, and by the lateral sacrococcygeal ligaments. The sacral canal contains a loose areolar tissue in which are embedded the filum terminale, the sacral and coccygeal nerves, and a rich plexus of veins.

PHYSIOLOGY

The pelvic and perineal floors are innervated by the second, third, fourth, and fifth sacral nerves and the coccygeal filaments. Both the sensory and motor fibers of these are anesthetized in the sacral canal and, as in spinal anesthesia, the sensory nerves are more readily affected due to their lower threshold for paralysis.

The uterus is innervated by both an intrinsic and an extrinsic nerve supply. The intrinsic plexus, supposedly coursing in the myometrium itself, has been shown to be able to function inde-

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pendently of the extrinsic. This has been demonstrated both experimentally in laboratory animals and clinically by the uneventful progress of labor in patients with paraplegia due to cord tumors, transection, or other spinal cord accidents. The intrinsic nerves are influenced by certain factors important for the institution of labor. The hormones, estrogen and progesterone, elaborated by the ovary and particularly the placenta in pregnancy and pitocin, produced by the posterior pituitary, are necessary for the induction and sustenance of co-ordinated contractions of the uterus. Similarly is the intrinsic supply affected by the mineral ion concentration, particularly of calcium, potassium, and magnesium.

In contrast, the extrinsic innervation of the uterus is derived from both the sympathetic and parasympathetic (cerebrospinal) systems, each of which transmits sensory and motor fibers.

The sympathetic fibers are principally motor in function. Originating in the solar plexus, these fibers traverse the superior mesenteric into the inferior mesenteric plexus, where they unite with fibers from the lumbar sympathetics to form the superior hypogastric plexus (presacral nerve). (That this nerve contains sensory fibers is evidenced by the fact that its resection affords relief in primary dysmenorrhea. However labor following excision of the superior hypogastric plexus is unaltered.) The superior hypogastric plexus divides to form the bilateral inferior hypogastrics, the hypogastric nerves, which pass downward and laterally furnishing the main sympathetic root for the pelvic plexus (the uterovaginal plexus, cervical ganglion, or the ganglion of Frankenhauer). Also contributing to the pelvic plexus are branches which are derived from the sacral sympathetic cords and the parasympathetic pelvic nerve, the nervus ergens. This parasympathetic supply to the uterus, the ergens nerve, arises from the second to the fourth anterior roots of the sacral plexus.

From this brief discussion it becomes evident that the pain of labor of uterine origin as well as that due to the overdistention of the pelvic tissues comprising the lower portions of the birth canal, can and will be eliminated by anesthetizing the sacral nerves, as is done in caudal anesthesia, while uterine contractions can continue almost unaffected.

TECHNIQUE

The sacral hiatus is rather easily identified. With the right third finger placed on the tip of the coccyx, the right index finger is passed along the midline toward the sacrum, until the J verted V

shaped depression is palpated. The apex of this triangular site is defined by the fourth sacral spine, while its base is marked by the two lateral cornua. Since the sacrum is an immobile structure, the sacrococcygeal articulation can be recognized with the external finger when the coccyx is moved by a gloved finger inserted in the rectum. To verify the location of the sacral hiatus further one might visualize an equilateral triangle with the base line extending between the posterior-superior iliac spines and the apex falling directly over the site for puncture.

The position in which the subject lies for the injection is optional. In our series, both the lateral decubitus as well as the knee chest position were used with equal success. Although the patient is probably more comfortable lying on her side, the spine assumes a scoliosis, which makes recognition of the bony landmarks somewhat difficult. On the other hand, having the patient kneel, with the elbows drawn as close as possible to the knees, gives the back a symmetrical arch, enlarges the sacral hiatus and exaggerates the anatomical prominences, all of which further facilitate the procedure. Obviously the knee chest position is more embarrassing and awkward to the pregnant mother; yet, because of its many advantages over the lateral decubitus, it is the position given preference.

The anesthetic being used in our clinic is metycaine (*Gemina* 1/2 methyl-piperidino-propyl benzoate hydrochloride). It is a white powder readily soluble in water, alcohol, or chloroform. The solutions are stable and retain their potency after sterilization by heating and do not deteriorate on standing. Although experimentally metycaine is more toxic than procaine, clinically this finding has not been substantiated. In its favor it may be said that metycaine-produced anesthesia is more rapid in its onset and is more enduring than that produced with procaine, and that it is a solution with antiseptic properties of its own. Our results, with the use of a 2 per cent

aqueous solution of metycaine without the addition of drenaline, compare very favorably with those obtained by them, who have tried procaine alone in various dilutions, procaine with adrenalin, with sodium chloride, with sodium bicarbonate with quinine with quinine and urea hydrochloride with magnesium sulphate and in many other combinations. In our series, the quantity of the solution used varied from 10 to 30 cubic centimeters but for the most part (357 cases) 5 cubic centimeters was used.

The instrumentarium required consists only of a 5 cubic centimeter syringe and an 18 gauge

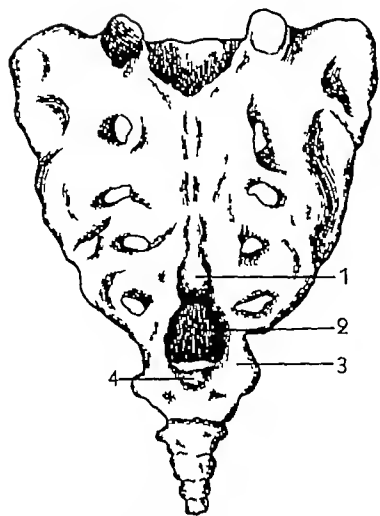


Fig 1 1, Fourth sacral spine, 2, sacral hiatus, 3 coccygeal cornu, 4, coccygeal tubercle

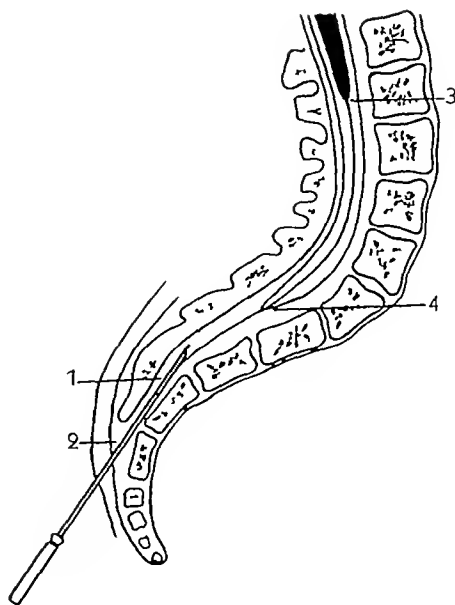


Fig 2 1, Sacral canal, 2, sacral hiatus, 3, end of spinal cord, 4, end of subarachnoid space

spinal puncture needle with stylet The operative field is prepared with tincture of iodine or other reliable antiseptic. The sacral hiatus is defined, and the needle is introduced practically perpendicularly into the sacral hiatus. Infiltrating the site for injection with a dermal wheel has been found unnecessary. Penetration of the fibrous sacrococcygeal membrane is announced by a sudden release in the resistance offered, and the point of the needle strikes the anterior wall of the sacral canal. It is then withdrawn a millimeter or two, and the hub is depressed gently, through an arc of approximately 70 degrees, so that the long axis of the needle lies practically parallel to the plane of the sacrum. It is then advanced 3 to 4 centimeters, to insure its presence in the canal. The stylet is withdrawn, the empty syringe is attached and aspiration is attempted. Withdrawal of spinal fluid or blood, signifying penetration of the subarachnoid space or of a vein is an indication for the removal and re-insertion of the needle. The solution is injected slowly, requiring about one minute for 25 cubic centimeters. The development of a tumefaction beneath the skin indicates a subcutaneous rather than an epidural infiltration. The injection completed, the patient is advised to resume the dorsal-recumbent position.

SUBJECTS

In this series of the first four hundred cases in which caudal anesthesia was used, 368 were primiparas and 32 were multiparas. Of the 368

primiparas, 293 were delivered by low forceps and episiotomies, 8 by midforceps and episiotomies (including 1 Duehrssen's incision), 28 were permitted to deliver spontaneously without an episiotomy, 10 delivered spontaneously with a perineotomy, 6 were forceps deliveries without episiotomies, and 20 were breech deliveries—in 4 of which the breech was broken up and extracted. In 17 cases, transverse blades were applied. In 15 of these, Simpson forceps were used, in 2, the Kjelland technique was followed. Seven occiput posteriors failed to rotate after two hours at complete dilatation. Two of these were delivered face-to-pubis, 2 were rotated with Kjelland forceps, 3 were turned, adopting the Scanzoni maneuver. One primipara was delivered by a low cervical cesarean section performed entirely under caudal anesthesia. In one version and extraction, the caudal block was found insufficient and was of necessity augmented by ether. Two of those delivered without an episiotomy sustained a first degree laceration. Two of the primiparas had twin pregnancies. Of the 32 multiparas, 9 had outlet forceps and episiotomies, 4 had a mid-forceps delivery, 3 were rotated by the Scanzoni operation, 8 were permitted to deliver spontaneously, 4 were delivered by low forceps without an episiotomy, and 2 had assisted breech deliveries. In one patient, caudal was administered for a Voorhees bag insertion, and in another a low

cervical cesarean section was performed entirely under caudal anesthesia.

In this series of 400 cases were 4 cardiacs, 2 patients with moderately advanced pulmonary tuberculosis, and 2 eclamptics.

RESULTS

Within the first 5 minutes after the anesthetic is administered, the outcries of the woman in the throes of labor are suddenly stilled, and the parturient, who only moments before had been writhing in pain, becomes quieted. Since the excitomotor reflex, due to pressure of the presenting part on the perineum, is abolished, the patient loses the urge to bear down. Instead, she becomes mentally at ease and physically comforted. Yet the rhythmic uterine contractions continue painlessly with the same frequency and duration as before, although, it is our impression, somewhat diminished in their intensity. The last-mentioned observation is not reliable, we admit, since the impression was obtained only by palpating the contracting uterus and observing its effect on the progress of labor. Several minutes after analgesia is obtained, anesthesia of the perineum develops. In tests for the loss of cutaneous sensation, which were made by grasping the skin with an Allis forceps, the development of anesthesia was consistently found to begin in the region of the anus and then spread fanwise upward toward the symphysis pubis, backward over the sacrum and gluteal regions, and laterally along the inner aspects of the thighs—the sum effect being a typical ‘saddle’ anesthesia. Simultaneously the musculature of the pelvic and perineal floors becomes completely relaxed. Even in primiparas, the lubricated examining hand can easily be admitted for such obstetrical manipulations as manual rotations, decompositions, and the like. Such relaxation greatly facilitates the application of forceps and reduces the incidence of vault tears. Sensation in and control of the lower limbs is unaffected. Caudal anesthesia has no effect whatsoever on the fetus. Furthermore, the third stage of labor is unaltered, as in only one instance was more than a simple Credé of the uterus necessary for the expression of the placenta. We believe, in fact, that the blood loss is less than that accompanying a delivery under ether anesthesia, since the relaxing effect of the ether on the myometrium is absent. The return of sensation occurs inversely to the direction in which it extended—beginning at the periphery of the saddle zone and advancing concentrically toward the anus. The postpartum period is unaltered.

In all but 13 of this series, the anesthetic was administered at complete cervical dilatation. In the first of these, it was given to a multipara 13 centimeters’ dilatation, to determine the effect on the progress. This was our first failure. In the second, it was administered at 6 centimeters’ dilatation, with the anterior lip of the cervix impinged between the advancing head and the symphysis pubis. The edematous cervix was liberated and forceps were applied. In the third and fourth cases, primiparas, fetal distress became evident at 6 and 8 centimeters dilatation, respectively. Manual dilatation was done and the infants were delivered with midforceps. The fifth case was a sextigravida, with an acute upper respiratory infection. The caudal block was done at 8 centimeters dilatation, and she was permitted to deliver spontaneously. In the sixth case, a primipara, low forceps were applied earlier because of increasing signs of maternal exhaustion. In the seventh case, labor was terminated at 1 centimeters dilatation because of a co-existing lobar pneumonia. In the eighth and ninth cases, multiparas, forceps were applied through an almost completely dilated cervix, because of breech disease; neither of these two had ante-partum cure; one was admitted in labor with anterior fibrillation and the other with mitral heart disease, gave a history of having been decompensated during the second trimester. In the tenth case a primipara, progress in the first stage was arrested in midpelvis by an obstructing calcified vaginal cyst. In the eleventh case, the cervix was undilated. A Voochees bag was inserted to institute labor medical induction having failed. The twelfth and thirteenth cases were elective cesarean sections and naturally the cervix were not dilated at the time.

Obstetrical analgesia, morphine and scopolamine, was administered to only 110 of the 400 cases. The omission of a narcotic was purposeful, since competent and reliable co-operation of the patient was desired in so far as volunteering accurate information as to the subjective effects of the caudal block on uterine and perineal pain.

Complementary anesthesia ether was given to 22 of the patients. Eleven were the cases in which the caudal block had failed completely. Ten experienced traction pains during forceps delivery necessitating ether for the delivery of the head only; the episiotomy repairs were done under the effects of the caudal block. In 1 case complementary ether anesthesia was required when it was found that the caudal block gave insufficient relaxation for an internal podalic version and extraction.

QUANTITY OF SOLUTION

In 10 of the patients, 20 cubic centimeters was injected, in 5 cases, 50 cubic centimeters was used, in 27 cases, 35 to 40 cubic centimeters administered, in 1 instance, only 10 cubic centimeters was given, in the remaining, 25 cubic centimeters was used. The patient who had received only 10 cubic centimeters experienced sufficient "traction" pain to require complementary ether. Generally speaking, for ordinary obstetrical procedures, no advantage was observed when either greater or lesser quantities than 25 cubic centimeters was injected.

ONSET OF ANESTHESIA

The shortest latent period between the time of administration of the anesthetic and the time when anesthesia became evident about the anal region was 2 minutes, the longest was 20 minutes, the average of the series was 7.4 minutes. Generally speaking, it was observed that approximately the same period of time was required for the complete extent of the anesthesia to develop from the time it first became evident, as had elapsed from the time the solution was injected to the time anesthesia was first noted.

DURATION OF ANESTHESIA

The longest period of anesthesia was 3 hours, the shortest, 36 minutes, the average for the series was 1 hour and 29 minutes.

AREA ANESTHETIZED

Consistently, the area over the sacrum and the gluteal regions, as well as the inner aspect of the thighs, was anesthetized, but the height to which the anesthesia rose on and above the vulva varied. Imagining the length of the vulva from the fourchette to the symphysis pubis being trisected into equal zones, it was found that when 25 cubic centimeters of metycaine was injected only the lowest (posterior) zone was affected in 1 case, only the two lower zones in 16 cases, and that the anesthesia extended up to and including the clitoris in 34.3 of the remainder. In 3 cases, anesthesia was observed to have extended from the level of the tenth dorsal spine to the toes, in 3 cases, it included the area from the level of the xyphoid to the knees.

That the quantity of solution injected has a definite relationship to the height to which the anesthesia rises on the anterior abdominal wall is evidenced by the fact that, except for 2 cases in which it did not ascend beyond the symphysis pubis, all 32 cases in which 35 cubic centimeters or more of solution was administered developed

anesthesia to the level of the umbilicus or higher, in several cases, in fact, it rose to the level of the xyphoid. Therefore, we conclude that, with the larger quantities, the anesthetic solution dissects its way under pressure in the extradural space to bathe the nerves at higher levels in the spinal column.

Taking advantage of this phenomenon, which we have discovered only in the recent past, we have extended the use of caudal anesthesia in obstetrics to cesarean sections, and in the gynecological service we have adopted it for selected laparotomies.

RESULTS

We were able to classify our results as follows:

- ++++ (4 plus) Anesthesia of the perineum. Loss of contraction pain.
- +++ (3 plus) Anesthesia of the perineum. Patient aware of contraction pain.
- ++ (2 plus) Anesthesia of the perineum. Loss of contraction pain. Patient experienced pain when traction with forceps was applied.
- o (o) Complete failure.

Guided by these criteria, the results could be grouped numerically as follows:

Cases	
++++ (4 plus)	34.8
+++ (3 plus)	31
++ (2 plus)	10
o (o)	11

Failures are usually due to inability to locate the sacral hiatus. Very obese women, in whom thick, soft tissue pads obscure the anatomical landmarks of the back and patients with deformities of the lower spine are, obviously, poor candidates for even an attempt at caudal block.

EFFECT ON VASOMOTOR SYSTEM

Realizing the occasional untoward effects of spinal anesthesia on the blood pressure, the influence of the epidural infiltration was closely watched. Sphygmomanometer and pulse readings were taken before the injection, during, and after, the delivery. Variations were inconsistent. In the greater number of cases, the blood pressure had not fluctuated more than 15 millimeters of mercury, in a few, the pressure had risen, in a few, a fall was observed. Other than the normal variations, i.e., the rise accompanying the pains and the expulsion efforts of the delivery, and the fall upon its termination, no remarkable influence of the metycaine on the blood pressure was noted. Similarly, no consistent abnormal influence of the caudal block on the maternal pulse was observed.

SIDE EFFECTS

Immediately after the injection of the anesthetic agent had been completed, 5 of the patients developed transitory episodes of disorientation accompanied by clonic convulsions, most marked in the upper extremities. The longest seizure lasted a minute, following which, as with the others, labor was completed uneventfully. Five others became disoriented and apprehensive for several minutes after the administration of the drug. No tremors or convulsions accompanied their reaction. For want of a more satisfactory explanation, we surmise that these reactions were due to individual sensitivity to the drug. The untoward vasomotor respiratory and gastro-intestinal symptoms and signs, such as tachycardia, palpitation, hyperpnea, pallor, nausea and vomiting, as reported by others, were not observed in any of our series. It is our deduction that such side effects may well be due to the epinephrine which the others had added to their anesthetic agent.

CONCLUSIONS

Caudal block offers a feasible and efficacious anesthesia for operative obstetrics. It permits the uterus to contract painlessly. It relaxes the pelvic floor and anesthetizes the perineum. It is harmless to both the parturient and her newborn. It permits the normal separation of the placenta and involution of the pelvic organs. All the untoward side effects of inhalation anesthesia are absent—there is no excitement stage, no nausea or vomiting, no danger of explosion. It lends itself well to an obstetrical service in which drop-ether possibly administered by an untrained interne or nurse, is the only other available anesthesia. It can be used without fear in patients with pulmonary, cardiac, or renal complications.

The accompanying drawings are by Mr. Leo C. Massopust.

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PUTRID EMPYEMA

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IN most discussions of suppurative pleuritis little or no distinction is made in the treatment recommended for various bacteriological types of pyogenic empyema. Only tuberculous empyema is considered as a distinct entity. Yet due to certain differences in the pathology of an anaerobic empyema from that of an aerobic infection of the pleural cavity, important modifications in the plan of treatment are necessary for the former group. Clinically it is easy to differentiate an aerobic from an anaerobic empyema in most instances. The common aerobic pleural infections yield purulent fluid which has no offensive odor. The pus in anaerobic pleural infections is usually very foul, and for this reason anaerobic empyema is also called putrid empyema.

The importance of certain fundamental principles in the treatment of aerobic empyema has been definitely established. The necessity of avoiding open thoracotomy in the early stages of a suppurative pleurisy has been stressed because it may lead to collapse of the lung and mediastinal displacement. After the suppurative pleuritis has been present for a sufficient length of time, the inflammatory reaction causes stabilization of the mediastinum and fixation of the lung, and open thoracotomy is then well tolerated. Observations on the thickness, specific gravity, or amount of sediment of the aspirated fluid have been used as clinical guides as to the time when open thoracotomy could be safely employed. Therefore, in general we regard the thickness of the pus as a criterion of the degree of mediastinal stability and pleural thickening. Although these observations on the pus are a very useful and valuable clinical guide in the treatment of aerobic empyema, the dictum to delay open thoracotomy until the pus is thick should not be applied to anaerobic empyema. Early open thoracotomy is indicated in anaerobic empyema regardless of the consistency of the purulent fluid. In putrid empyema the pus may remain thin for a long time. The marked toxicity of many of these patients, due to the type of pleural infection present, necessitates early drainage. The fact that the pus in anaerobic empyema continues to be thin for a considerable time in some cases does not mean that little pleural thickening is present or that the mediastinum fails to stabilize. *In anaerobic empyema the con-*

sistency of the pus is an unreliable guide as to when open thoracotomy may be performed with safety. As the anaerobic pus causes marked toxicity, and as repeated aspiration of the foul fluid with a needle is very dangerous because of the frequency of severe thoracic wall infections, these cases must be treated somewhat differently than aerobic empyema. This does not mean that the same fundamental principles of treatment are not applicable to both aerobic and anaerobic empyema, the principle of avoiding mediastinal flutter and pulmonary collapse applies to all cases of empyema. In anaerobic pleural infections, however, the thickness of the pus and mediastinal stability are not closely correlated due to the pathology of putrid empyema. Neuhof and Hirshfeld (3) emphasized the importance of recognizing putrid empyema as a distinct type of pleural infection because of the special pathology and therapeutic problems involved. They recommended early surgical drainage by open thoracotomy as the preferred method of treatment.

During a period of 2 years (1939-1940) 23 cases of putrid empyema were treated on the thoracic surgery service of Kings County Hospital. This group does not include any cases of anaerobic empyema following surgical intervention in the thorax.

Besides the group of cases analyzed in this paper the authors have observed a considerable number of cases of putrid empyema in other clinics. The poor results obtained when thoracotomy was delayed prompted the present study and plan of therapy.

Age. The patients in our series ranged from 19 to 72 years of age. Nineteen of the 23 cases occurred in the age group from 30 to 70. The average age of the patients was 47 years. The condition was encountered most frequently in the sixth decade of life. Although there were no cases of putrid empyema in children in this series, the condition does occur in childhood. Neuhof and Hirshfeld (2) reported 17 cases of anaerobic pleuritis in a series of 184 cases of empyema in children. The therapy for children and adults is similar.

Sex. In our series 20 of the 23 cases, or 87 per cent, were males, and 3, or 13 per cent, of the cases were females.

ETIOLOGY

Putrid empyema is usually secondary to intra pulmonary disease. Bronchiectasis, pulmonary abscess, and suppurative pneumonia are the most common primary conditions. Anaerobic empyema may also result from perforation of the esophagus, mediastinitis, and penetrating wounds of the thorax, or follow surgical contamination of the pleural cavity during lobectomy pneumococotomy or drainage of a pulmonary abscess. A foul empyema may also be secondary to a subphrenic infection which has perforated the diaphragm. In these latter cases, however, a somewhat different group of bacteria are encountered.

The almost constant association of foul dental sepsis with putrid empyema secondary to intra pulmonary disease led one of us (E. J. O.) to associate with the late Dr. C. Coulter to study the bacteriology of the pyorrheal pockets and the material from the intrapulmonary lesion. In a small number of cases the same organism, a very virulent anaerobic haemotoxin-producing streptococcus, was isolated from both lesions. Dr. Coulter's untimely death interrupted this work, however, he believed that this organism acted as a singularly virulent factor in producing anaerobic intrathoracic suppuration.

In many cases of ruptured pulmonary abscess a putrid pyopneumothorax results due to a free communication between the empyema and the intrapulmonary abscess cavity and hence with the bronchial tree. The etiology of the pleural infection in this group is obvious. There is another group of cases in which no bronchopleural fistula is present. In this latter group the pleural infection is probably due to the rupture of a minute subpleural abscess, which is so small that no bronchial communication with the empyema cavity is established. The pleura is infected by a direct extension from a similar type of infection in the underlying lung. More or less extensive pneumonia may be present. In a considerable percentage of these cases there is a history of bronchiectasis preceding the acute illness. In most instances in which such a history is lacking, the infection in the lung and secondarily in the pleural cavity is due to aspiration of infected secretions from the mouth and upper air passages.

A mixed bacterial flora is usually present in anaerobic empyema. Fusiform bacilli, spirochetes, and anaerobic streptococci are the most frequent findings. Other organisms, including aerobes, may also be present. Symplosta seems to be an important factor in the action of these organisms. It has been shown experimentally by

Smith that a combination of organisms is necessary to produce a foul-smelling abscess in man.

In every case in our series in which anaerobic cultures were made, anaerobes were demonstrated to be present in the pus. Streptococci were the most frequently demonstrated organism, both as the aerobic and anaerobic cultures. Hemolytic streptococci were found more frequently than nonhemolytic streptococci in both the aerobic and anaerobic cultures. *Staphylococcus aureus* was also frequently present and often grew both aerobically and anaerobically. Fusiform bacilli were frequently demonstrated on direct smear of the pus and sometimes on culture. *Spirilla*, *Staphylococcus albus*, *Bacillus proteus*, *Bacillus subtilis*, pneumococci, bacilli of the colon group and some unidentified bacteria were also found.

SYMPTOMATOLOGY

On the basis of their history cases of putrid empyema may be divided into two groups. In the one group there is expectoration of foul sputum which indicates the presence of an anaerobic suppurative process. The sputum may come from an intrapulmonary focus, such as a pulmonary abscess or bronchiectasis, or from an anaerobic empyema with bronchopleural fistula. In the second group the foul sputum is absent and the symptoms may suggest an ordinary pneumonia rather than a suppurative process either in the lung or the pleural cavity.

The majority of cases of putrid empyema have a history of previous intrapulmonary infection. There may be a history of a chronic productive cough, and the sputum may be purulent and at times foul. These are mostly cases of chronic bronchiectasis or chronic pulmonary abscess. In other cases the history suggests an acute pulmonary abscess which then ruptures into the pleural cavity. The severity of the symptoms at the time the empyema develops depends chiefly on whether a localized or extensive empyema results. When the perforation of the pulmonary abscess is into a localized portion of the pleural cavity there may be little change in the patient's symptoms. When an anaerobic abscess ruptures into the free pleural space, the symptoms may be very acute and the patient's condition becomes rapidly worse. In some instances the patient may no longer raise sputum due to drainage of the contents of the abscess into the pleural cavity.

In those cases of putrid empyema without a history of acute pulmonary suppuration, the symptoms suggest a pneumonia. The acute illness is usually characterized by malaise, fever and pain in the chest. There may be a cough which is

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dry or productive of mucoid sputum, sometimes cough is absent. Occasionally the sputum is rusty or frankly bloody.

A definite history of chronic cough preceding the acute illness was recorded in slightly over half of our patients. We feel, however, that if the history had been more carefully taken, a considerably larger percentage of patients would have been found to have had a cough before the acute illness. In some instances the cough was productive of purulent sputum, but only a few patients gave a history of foul expectoration in the past. Several patients had had previous attacks of pneumonia, and one patient had pneumonia repeatedly. In one instance the pulmonary disease dated back to a foreign body which had remained in the bronchus for several months before it was removed endoscopically 18 months prior to the development of the empyema.

DIAGNOSIS

When a putrid empyema is secondary to an acute pulmonary abscess, the diagnosis is usually not difficult if the intrapulmonary focus has suddenly ruptured into the free pleural space. More frequently, however, there is only an encapsulated empyema associated with the pulmonary abscess, and the diagnosis may be difficult to make. The change in physical signs and roentgen studies may indicate the presence of a secondary empyema. Sometimes the co-existing empyema is diagnosed only at the time of thoracotomy.

It is in the cases of putrid empyema without evident previous intrapulmonary suppuration and without foul sputum that the diagnosis is often delayed. At the time of onset of the acute illness a diagnosis of pneumonia is usually made. Certain atypical features may be noted. The sputum may not be rusty, and although a lobar pneumonia is frequently diagnosed, it may be found difficult to type the sputum. Early in the course of the illness the physical signs may suggest the presence of pleural fluid. Roentgenograms may reveal findings consistent with pneumonic consolidation or pleural effusion. The density is frequently interpreted as pulmonary consolidation when it is chiefly due to pleural fluid. The mediastinum is less likely to be displaced in anaerobic empyema than in aerobic empyema because previous pulmonary disease is frequent in the former group and tends to fix the mediastinum.

Most of the patients in our series gave a history of a rather sudden onset to the acute illness. Chest pain was complained of at some time in almost every case. Twenty of the 23 patients had a cough. In 13 cases the cough was productive, but

only 5 patients had foul sputum. In each case of foul sputum there was either an associated pulmonary abscess of appreciable size or a bronchopleural fistula. Only 3 patients had bloody sputum.

A preliminary diagnosis of pneumonia was made in most of the cases. In 4 instances, a pulmonary abscess was diagnosed. Over half of the patients received one of the sulfonamide drugs before the diagnosis of empyema was made. These chemotherapeutic agents do not give the typical dramatic response in this type of infection. In fact the failure to respond to the sulfonamides is a point in the differentiation of the atypical pneumonia associated with a foul empyema from the typical pneumococcus pneumonia. About half of the patients were regarded to be critically ill at the time of admission to the hospital.

The diagnosis of putrid empyema is definitely established by the aspiration of foul pus or foul air from the pleural cavity. Due to the previous intrapulmonary disease causing pleural adhesions, the empyema may be somewhat loculated. We have seen considerable delay in making the diagnosis in several cases due to an anterior location of the empyema. Low aspiration should be avoided because the diaphragm may be elevated as a result of the previous intrapulmonary disease. If the needle traverses the diaphragm, subphrenic infection may result. A spreading subphrenic infection due to this cause was present in one of our cases and it has also been observed by Neuhoef and Hirshfeld (3). A similar complication in aerobic empyema is very unusual. In 2 instances in which the diagnosis of a putrid empyema was made very early, the aspirated fluid was clear and serous, but the overlying air was foul. The odor is therefore present early.

Smears of the aspirated fluid should always be done, usually a variety of organisms will be found. Special examination with the darkfield microscope should be done for spirochetes. Aerobic and anaerobic cultures should be planted. Improper and incomplete examinations of the pus may result in a failure to identify the anaerobic organisms, and hence the occasional laboratory report that this foul fluid is sterile! One does not need to await the report of the culture of the pus, however, to know that immediate surgical intervention is indicated. If tuberculosis were also present, open thoracotomy would still be indicated except in rare instances.

TREATMENT

The importance of immediate treatment in cases in which an anaerobic pulmonary abscess

has ruptured into the free pleural space has been recognized for some time. These patients are best treated by open thoracotomy.

In an anaerobic empyema without clinically demonstrable pulmonary abscess and without bronchopleural fistula, there is usually unwarranted delay in instituting proper therapy. Open thoracotomy with rib resection should be performed as soon as the diagnosis of putrid empyema is confirmed by aspiration. There may be a rare case in which it may be advantageous to delay the thoracotomy for a day or two because of a massive fluid accumulation with mediastinal displacement. In such an instance an incision under local anesthesia should be made through the skin, subcutaneous tissues, and deep muscles of the thorax down to the ribs and intercostal muscles at the site of the exploratory aspiration. This incision should be made within a few hours of the first aspiration. Further aspirations are done through the open wound, which is packed with zinc peroxide gauze. Of course some cases of anaerobic empyema may be aspirated repeatedly without a thoracic wall infection developing but the incidence of infections following thoracentesis is quite high and, when once developed, the thoracic wall phlegmon is of such severity that aside from intrapulmonary disease it is the most important factor in the mortality in these cases. This is entirely different from the situation in aerobic empyemas, in which, with proper technique, infection in the thoracic wall is relatively uncommon following thoracentesis, and, if infection develops, it can usually be easily controlled by simple measures.

The reasons for the serious and frequent thoracic wall infections with anaerobic empyema are several. The pus is often watery in character and, therefore, can leak through a small needle track. Secondly we are dealing with anaerobic organisms which are likely to gain a foothold in a puncture wound in which conditions are favorable for their growth. The ease with which appreciable amounts of this infected fluid leak through the needle track in the intercostal muscles has been convincingly shown at operation when the pleural cavity is needled after the chest wall incision has been carried down to the ribs. The fact that gross leakage of the pus occurs and that it gravitates downward from the puncture site beneath the deep thoracic muscles is shown by the location of the infection in the thoracic wall, which may extend almost entirely in a downward direction from the aspiration site.

Surgical drainage of thoracic wall infections following aspiration of an anaerobic empyema

may be delayed because a cellulitis rather than an abscess is diagnosed. The pus usually collects just outside the ribs and beneath the thoracic muscles. Therefore tenderness and some swelling may be the only indication of chest wall infection. Redness of the skin may be absent. Fluctuation is usually not demonstrable because of the deep site of the purulent collection. For these reasons several days may elapse before the chest wall infection is considered ready for incision and drainage. By this time extensive gangrenous infection of the deep tissues of the thoracic wall may be present. We have seen extensive necrosis of the tissues within a day of a thoracentesis which yielded thin foul pus. The periosteum of ribs and scapula may be destroyed with resultant osteomyelitis.

As mentioned previously with very few exceptions, a thoracotomy with rib resection is performed under local anesthesia as soon as the diagnosis is made. The patient is placed in such a position on the operating table as not to flood his bronchial tree with pus in those cases with free bronchopleural communication. In a considerable number of cases the only safe position is with the patient sitting upright. The surgeon himself should supervise the placing of the patient on the operating table so the proper position for that particular patient may be chosen.

A long incision is made through the area of aspiration. Care is taken not to undercut the muscles. A rather long segment of one or occasionally more ribs is removed. The empyema cavity is opened cautiously because of the possibility of pulmonary collapse. Although the mediastinum is usually stable, precautions must be taken in the event that this should not be the case. If there is sucking of the wound associated with mediastinal shift, the patient should be promptly rolled over onto a large wet dressing as this will markedly diminish the flow of air through the opening. Although we have always been prepared to do this, so far we have not found it necessary. The pus is removed by suction and the presence or absence of bronchial fistula noted. Occasionally the opening into a pulmonary abscess is enlarged. Large rubber tube drains are inserted. It is imperative that no sutures whatsoever are inserted in the thoracic wall. A single suture inserted for the purpose of anchoring a drainage tube may result in a spreading thoracic wall infection of a serious nature. Adhesive strapping may be employed instead. The edges of the wound should not be strapped, as the large opening is a great asset. The chest wall wound is packed with gauze soaked in zinc peroxide. In small empyemas

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cavities without bronchopleural fistula, zinc peroxide has also been placed in the pleural cavity. Zinc peroxide is of great value in the treatment of anaerobic thoracic infections (1).

Twenty-two of the 23 patients in this series were treated by thoracotomy with rib resection and open tube drainage. Two of the patients had an incision made in the chest wall down to the ribs a few days before the open thoracotomy was done. In one case the pleural cavity was not drained surgically because this patient died in diabetic acidosis a few hours after a phlegmon of the chest wall was drained.

Because of previous unsatisfactory results when open thoracotomy was delayed in cases of foul empyema, most of the patients in this series were treated by rib resection shortly after the diagnosis was made by thoracentesis. Half of the patients were operated upon within 24 hours of the first aspiration. The delay in most of the other cases was due to the fact that the patient was not immediately transferred to the surgical service. Eighteen of the 23 patients had only a single thoracentesis before thoracotomy. Two patients were aspirated more than twice, both of these patients died.

At the time of open thoracotomy the pus was thin in 9 cases and thick in 14 cases. The lung was partly adherent to the lateral thoracic wall in 17 of the 23 cases. In the remaining cases the empyema was extensive. In 8 of the 9 cases in which the pus was thin at the time of thoracotomy, the lung was prevented from complete collapse by adhesions to the thoracic wall. In the single case in which the pus was thin and the lung was not adherent when thoracotomy was performed, the lung re-expanded well after operation. Therefore, in this series of cases the drainage of putrid empyema when the pus was thin did not result in any difficulty with mediastinal shift or late re-expansion of the lung.

Chest wall infections developed before thoracotomy in 4 of the 23 cases, or an incidence of 17 per cent. This does not give a true picture of the danger of this complication in putrid empyema, however, because most of the cases in this series had a thoracotomy performed shortly after a single aspiration. Three of the four thoracic wall infections developed after a single aspiration and were clinically manifest within 24 hours of the only thoracentesis. The other case had three aspirations performed. Two of the 4 patients with phlegmons of the thoracic wall died. Both of these fatal cases also had diabetes mellitus, and the chest wall was not drained until 4 days after the thoracentesis. In the 2 cases with chest

wall infection that recovered, the thoracic wall was drained the day following the chest aspiration. In 3 of the 4 cases of phlegmon the fluid aspirated from the pleural space was thin. In the single case with thick pus, many fusiform bacilli and other anaerobes were found in the purulent material.

Various complicating conditions were present in addition to the pulmonary and pleural infection. Two patients had diabetes mellitus. Four patients were cardinals, and 2 of these were decompensated before thoracotomy. One patient had a toxic hepatitis and acute tonsillitis with cervical adenitis. Several had general arteriosclerosis and chronic nephritis.

POSTOPERATIVE COURSE

With proper early operation the prognosis is good as far as the pleural infection is concerned. The foul odor may be gone within 24 hours. The patient may show remarkable improvement. If there is extensive intrapulmonary suppuration, this will be the most important factor in prognosis. Oxygen therapy should be used freely.

The chest wall wound often has a necrotic appearance unless zinc peroxide packing is inserted into the thoracic wall wound. This agent is most effective in these anaerobic infections. Care should be taken to prevent the drainage opening from contracting down too quickly. The retention of a very small amount of pus may cause quite a febrile reaction. If a bronchopleural fistula is present, drainage should be prolonged.

The use of sulfonamides seems to be of benefit in some cases. We have employed chemotherapy in several cases in which there was a febrile course after operation apparently due to residual pulmonary infection. Before ascribing the fever to intrapulmonary disease, one must ascertain that the pleural drainage is entirely satisfactory. At the time of drainage of the empyema it may be difficult to evaluate the extent of the intrapulmonary suppuration. If putrid sputum persists after operation, it should be ascertained whether this comes from an undrained pleural pocket with bronchial communication or from the lung. Some mucoid sputum may persist for a considerable length of time.

Painful swollen joints have been present in several of our cases in the postoperative period. In 2 instances the joint pains were associated with fever for several weeks, but the onset of these symptoms was more than a month after adequate drainage of the empyema.

Most of the patients continued to be febrile for considerable periods of time after the empyema

was drained. This was thought to be chiefly due to the slow subsidence of the intrapulmonary infection. Less than half of the patients became afebrile within 3 weeks of thoracotomy. Several continued to be febrile for almost a month and in 4 cases the temperature became normal only from 6 to 7 weeks after the empyema was drained. In view of the slow subsidence of the intrapulmonary infection, and because we did not wish to discharge these patients while the empyema cavity was of sufficient size to require a drainage tube, the period of hospitalization was prolonged. Most of the patients remained in the hospital for a period of 2 to 4 months from the time of admission.

RESULTS

Three of the 23 patients died, giving a mortality of 13 per cent. One patient died as a result of multiple pulmonary abscesses and an extensive phlegmon of the chest wall which followed a thoracentesis done 4 days before the thoracotomy. This same patient also had an anaerobic subphrenic abscess on the same side and diabetes mellitus. Death was chiefly due to the extensive intrapulmonary suppuration. The second death occurred as a result of diabetic acidosis which was not controlled because of a chest wall phlegmon and an undrained anaerobic empyema. In this case we feel that early drainage of the empyema

before the chest wall became infected might have resulted in a successful outcome. The third death was also in a case in which thoracotomy was delayed, and there was an undrained pulmonary abscess.

All 20 patients who recovered obliterated the empyema cavity after thoracotomy and their wounds healed. None required any further surgical procedures as far as the empyema was concerned. Some of the patients continued to have chronic cough and sputum due to the persisting intrapulmonary disease.

CONCLUSIONS

1. Putrid empyema should be differentiated from aerobic empyema.
2. Thoracentesis in cases of putrid empyema is associated with considerable danger of a serious thoracic wall infection.
3. Early open thoracotomy is the treatment of choice in putrid empyema.

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MAMMARY CARCINOMA

A Review of 2,636 Cases

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TO augment the already voluminous and frequently repetitive literature on mammary carcinoma is an act which one should contemplate with considerable misgiving. More articles have been published on the subject of carcinoma of the breast than on any other single regional form of cancer. A greater number of radical surgical procedures have been performed for mammary cancer than for all types of malignant lesions of the entire gastro-intestinal tract (24). The accessibility of the breast, its predilection toward the development of both benign and malignant lesions, and the complex pattern of its hormonal control have made its problems a matter of interest to investigators in widely separated fields. Nevertheless, the accumulation of knowledge concerning mammary cancer has not produced any commensurate degree of agreement among research workers or clinicians as to its problems, either epidemiological, etiological, or therapeutic.

The present study is based on a review of 2,636 abstract clinical records of carcinoma of the breast in the cancer archives of the American College of Surgeons. Although the College established the cancer archives primarily as a repository for the abstract records of "cured" cancer cases, the material reported here includes 1,511 5 year "cures" and 1,125 cases in whom recurrences or metastases developed within the 5 year period. Contributed by many institutions and individuals in the United States and Canada during the past decade, this material is obviously not susceptible of analysis by methods used in the review of consecutive cases in a single institution. Any attempt to evaluate the therapeutic methods used in such a collected series would be particularly fallacious for this and other reasons meriting wider recognition.

The number of cases included in this study is sufficiently large to make possible an evaluation of certain factors of interest in the genesis, prognosis, and management of mammary carcinoma. The factors studied are seven in number: age, family history of cancer, childbearing, lactation, known duration of tumor, stage of disease at treatment, and the survival of "cured" cases after the 5 year

period. All of the cases included in this study are recorded as having had histological confirmation of some form of mammary carcinoma. Instances of sarcoma of the breast, and of carcinoma in the male breast, have been excluded. "Five year cure" cases are arbitrarily defined as those in whom a minimum period of 60 months has elapsed following treatment without clinical evidence of recurrence. Practically all of the records studied were submitted on the abstract cancer record form recommended by the cancer committee of the American College of Surgeons, the uniformity of which greatly facilitates this type of study. Unfortunately, as shown in Table I, the variability of detail in which the forms were completed proportionately determined the number of cases available for analysis of the several factors studied.

AGE

In Figure 1 is presented the comparative age distribution of 1,486 5 year cures and 1,045 recurrent cases, and, drawn to scale, the estimated current cases of mammary cancer by age groups in the white female population of the United States. Table II shows the detailed figures from which this graph was constructed.

The number of cases up to the age of 35 is not sufficiently large to be of real significance. There is, however, legitimate cause for interest in the 13 cases in which patients were under the age of 25 years. Ten of this group were 5 year cures and only 3 were recurrent cases. Most noteworthy is the slight but consistent percentage excess of 5 year cures over recurrent cases in the age period from 36 to 50 years. Past the age of 50, the percentage of recurrent cases is greater, and this unfavorable balance carries through to the most elderly group of 70 and over. The curves, both for the 5 year cures and the recurrent cases, roughly parallel those for the estimated current cases in the general population indicating that age is not an important prognostic factor in cancer of the breast.

Such a conclusion is in sharp conflict with a current attitude recently expressed by Pack and Liv-

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The expression "recurrent cases" is used throughout to designate cases in which recurrence or metastases appeared before the 5 year post treatment period elapsed.

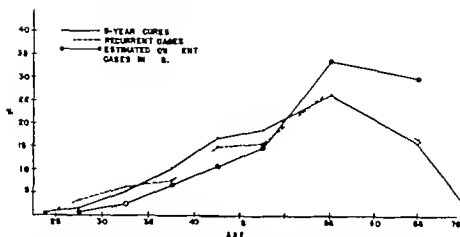


Fig. Percentage age distribution of 486 5 year cures and 1045 recurrent cases.

lignation that cancer of the breast is a much more menacing disease in young women than in mid life or old age. So general has this impression become that there seems to be an attitude in many clinics of adopting less aggressive therapeutic measures in patients under 40 years of age. The rapid course of inflammatory carcinoma of the breast, more common in younger women, and the gravity of mammary carcinoma occurring in the pregnant or lactating patient undoubtedly lend additional weight to this credence. One also has the impression that the statistics from specialized cancer institutions are weighted by the proportion of referred problem cases among younger women.

A number of studies of end results in general institutions have demonstrated that age has little bearing on prognosis (5, 10, 12, 18, 23, 28, 29). The balance of evidence, in fact, indicates a more favorable outcome for patients in the fourth than in the sixth decade. Evans and Leucutis, in a study of 1,300 cases, after corrections had been made for natural factors of longevity found a distinct excess of 5 and 10 year cures in the group under 40 years of age over those in the sixth decade. Lewis and Rienhoff studied the 10 year

end-results of surgical treatment at the Johns Hopkins Hospital from 1889 to 1931 and concluded that no essential variation could be shown for the age groups from 30 to 70 years. An analysis of percentage 5 year survivals¹¹ by age groups of 3,740 cases, reported by Harrington in 1935, also demonstrates the less favorable results of treatment in women of 55 to 64 years of age.

The evidence presented here strongly supports the contention that the best results in the treatment of breast cancer are obtained between the ages of 35 and 50. The thesis that an especial virulence exists for mammary carcinoma in the young is not verified.

HEREDITY

Information concerning the hereditary background of cancer patients gleaned from ordinary

TABLE II.—AGE IN 531 CASES

Age group	Five year cures		Recurrent cases		Current cases
	No. cases	Pct cures	No. cases	Pct cures	Pct cures
Less than 25	30				
25 to 30	24		24		27
31 to 35	77		65	6	27
36 to 40	132	20.2	80	2	6
41 to 45	153	17.0	56	5	19.5
46 to 50	166	12	266	2	14
51 to 55	207	26	203	26	24
56 to 60	127	18.0	176	17	20.2
61 or more	54	2.6	66	6	
	1,576	100.0	1,045	100	100

¹¹Interpolated

TABLE I.—CASES AVAILABLE FOR ANALYSIS OF SEVEN FACTORS IN 2 636 RECORDS OF MAMMARY CARCINOMA

Factor	Number of records with adequate data
Age	2,553
Family history of cancer	278
Fertility	87
Lactation	146
Duration of tumor	945
Stage of disease (5 year cures)	1,571
Survival of cured cases	1,553

TABLE III.—FERTILITY IN 1,817 CASES OF MAMMARY CARCINOMA

Nulliparae. No. children	1717 cases	Recorded cases
	400	34
	34	15
	145	117
3	79	06
4	53	64
5	30	56
6	21	20
7		
8	6	5
9	7	8
	4	4
		3
3	4	4
14		
5		
	805	923

number of children borne seems to have little or no influence in prognosis. These conclusions are drawn from the data presented in Table III.

LACTATION

Information concerning the functional activity of the breast was available in only 1,146 of the 1,636 records reviewed. Seven hundred and forty-two 64.8 per cent, of these patients were nulliparous, but this figure is heavily weighted by the paucity of information in the abstract records concerning lactation in parous women. In only 404 records of childbearing women was there any approach to satisfactory information concerning their lactation. In 234 cases, the statement "normal" lactation appeared, and such statements were accepted at face value. It is more than probable however that careful questioning will disclose many abnormalities of lactation in women who maintain uncertain recollections of "normal" lactation (1). One hundred and forty-two of these 404 parous patients either had failed entirely to suckle or during lactation had suffered such aberrations as "caked" breasts, abscesses, and periperal mastitis. Twenty-eight additional patients had nursed less than 3 months after one or more deliveries, compared to the 6 month period of lactation generally accepted as desirable. In practically all instances these abnormalities of lactation affected the breast which subsequently became the site of carcinoma, and in a considerable number the cancerous breast alone had been afflicted by inflammatory disease during lactation.

Using as a standard Wainwright's figure that 20 per cent of American women in a control series had not lactated, in Figure 3 is charted the lacta-

tion history of this group of cases. Setting with the 742 nulliparous cases, in 170, or 43 per cent of 404 parous women with breast cancer, the breast had failed properly to perform its physiological function of lactation.

Failure of normal lactation as a factor in the genesis of mammary cancer is a thesis which has received complementary verification from a number of clinical and experimental studies in recent years. Adair and Bagg (1) in a study of 200 cases, found only 8 per cent with accurate histories of normal lactation. Wainwright found failure of lactation in 40 per cent of 637 patients, compared to only 20 per cent in 541 control cases. Lee reported that 31 per cent of 156 breast cancer cases had never lactated, without mention of abnormalities in lactation. In a tribe of African aborigines whose women habitually nurse their children for 2 to 3 years, Ellis found that mammary cancer was a rare disease.

Notable experimental evidence on this subject has been adduced by Bagg and his co-workers. Bagg's "functional test" in mice consists of rapid breeding of females coupled with prevention of suckling by withdrawal of the litters as early as possible after birth. By this means strains of inbred mice with low spontaneous incidence of mammary cancer have developed a greatly increased ratio of such tumors. In C 57 strains of mice which apparently had not developed a mammary tumor in 10 years of inbreeding the functional test produced mammary tumors in 15 per cent of the animals subjected to this form of physiological stress. Bagg has further increased the incidence of mammary carcinoma in animals by ligation of the terminal ducts. The consequent stasis and ductal distention led to changes in the ductal epithelium which eventually gave rise to infiltrating carcinomas.

Such experimental and clinical evidence as has been presented makes possible the statement that failure of the breast to perform properly its physiological function is the most consistent apparent factor in the genesis of human mammary carcinoma. Whether the actual etiological factor is mechanical, due to distention of ducts and retention of secretion (19) or chemical, originating in retained products of lactation or in repeated hormonal stimulation, is beyond the scope of this discussion. Such analyses as are reported here and elsewhere notably by Adair (1) may well lead one to regard normal lactation as a measure of prophylaxis against carcinoma of the breast of which obstetricians and pediatricians should be cognizant. There is a well recognized tendency particularly among urban women, to shirk the

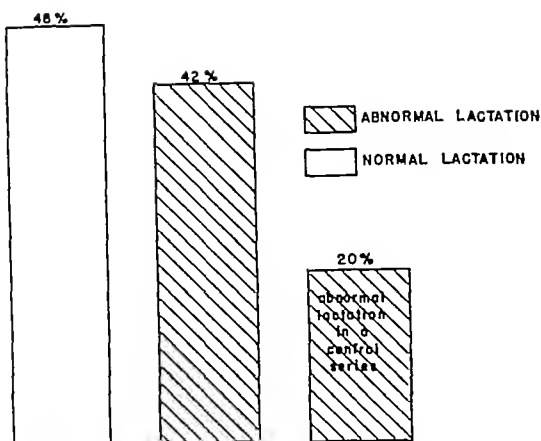


Fig 3 Lactation history in 404 parous patients

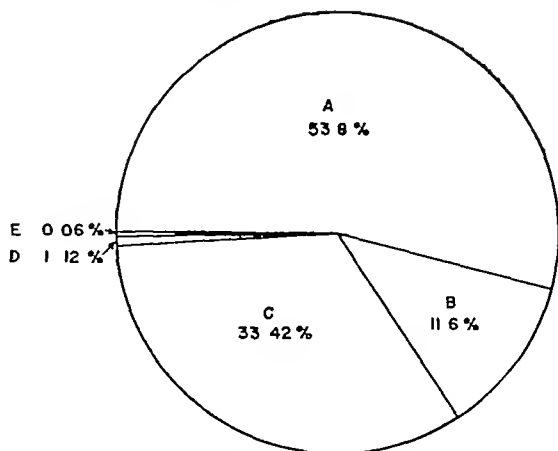


Fig 4. Stage of disease at treatment in 1,511 5 year cures

duty of breast feeding, and the frequency with which this practice is condoned and even recommended by physicians is to be deplored. It is entirely possible that the steadily increasing incidence of breast carcinoma in "civilized" women is in large measure due to complete or partial failure of lactation.

KNOWN DURATION OF TUMOR

In Figure 4 is graphically shown the known duration of the breast tumor from first recognition by the patient to treatment in 938 five year cures and 1,007 recurrent cases. The importance of early treatment is well illustrated in the sharp decline in the number of cases amongst the 5 year cures treated from 1 to 11 months after recognition of the tumor. Over the same period of increasing delay, the number of recurrent cases is generally though not consistently greater than that of 5 year cures. It is, however, the institution of treatment within the first 2 months that apparently produces the most appreciable increment in 5 year cures. With a delay of 12 months and over, both groups again show a sharp increase, with the recurrent cases in excess. The appreciable proportion of 5 year cures, 24.8 per cent, treated more than 1 year after the recognition of the tumor probably has a twofold explanation. Most obvious is the fact that the majority of these cases represent the indolent, slowly growing breast carcinomas of low degree malignancy which metastasize late, or occurring in hosts whose desmoplastic reaction to the tumor is intense. More debatable is the concept that some of these carcinomas arose in pre-existing benign lesions of the breast as suggested by the presence of tumors for periods as long as 5 years among the cured cases.

In those patients treated within 12 months after recognition of the tumor, the average period of delay was 3.08 months for the 5 year cures and 4.5 months for the recurrent cases. Of the 5 year cures, 44.6 per cent were treated within 3 months of recognition of the tumor, while 34.2 per cent of the recurrent cases were treated with equal promptness. Treatment was instituted more than 1 year after the tumor was noted in 24.8 per cent of the 5 year cures and 33.3 per cent of the recurrent cases. Thus there is a definite inverse relation between delay in treatment and chance of cure, though not as pronounced as one might expect.

Otherwise stated, 44.6 per cent of the 5 year cures were treated within 3 months, and 28.5 per cent 12 months or more after recognition of the tumor. Thus 73.1 per cent of all of the 5 year cures were treated either very early or very late, lending point to the natural division of breast cancer into 2 general groups: those which metastasize early and those which remain a localized disease for long periods of time. Recognizing in addition the fact that in a certain proportion of the cured patients treated early the tumors are of the slow growing type, one is confronted with the conclusion that in spite of the importance of early treatment in eradicating certain early lesions, end-results are determined more by natural selection than by early treatment. In general terms, this analysis indicates that of every 4 instances of 5 year cures of carcinoma of the breast, 2 are treated within 3 months, 1 from 9 to 12 months, and 1 more than 1 year after recognition by the patient.

FIVE YEAR "CURE" CASES

Stage of disease at treatment The stage of the disease at the time of treatment in the 1,511 cases

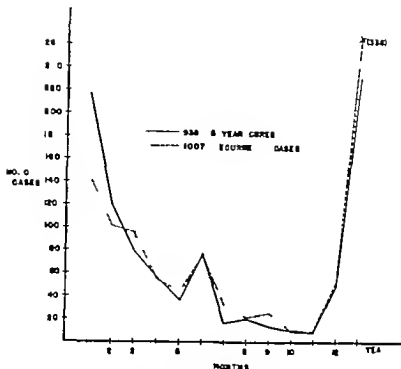


Fig. 5. Known duration of tumor

of 5 year cures is shown in Figure 5. The classification used is that recommended by the cancer committee of the American College of Surgeons

Stage A. Disease limited to breast.

Stage B. Questionable involvement of axillary nodes.

Stage C. Axillary nodes involved.

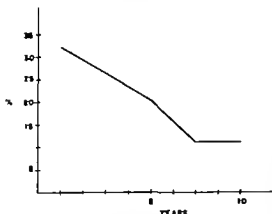


Fig. 6. Percentage distribution of 569 cases, 6 to 10 years

Stage D. Supraclavicular nodes involved.

Stage E. Remote metastases present.

In this study only those cases in which there had been microscopic confirmation of axillary node metastases were classified as Stage C. In 175 cases, 11.6 per cent, the records failed to provide adequate information on this point, and in view of the known inaccuracy in clinical judgment as to the presence or absence of axillary involvement (11) these cases were designated as Stage B.

The feature of interest in these figures is that 33.4 per cent of this large number of 5 year cures were histologically proved to be Stage C cases, a fact of the greatest clinical importance. Further,

majority of the cures classed as Stage B were those in which the presence of clinically positive axillary nodes was recorded but in which the microscopic confirmation was lacking. If one accepts Greenough's statistics that 90 per cent of the clinical Stage C cases are confirmed by the pathologist as such, then the proportion of Stage C cases in this cured group will approach 40 per cent. One series has been reported in which 50 per cent of 5 year survivors were Stage C cases (21). The inference is plain that to deny patients with operable growths the chance of radical treat-

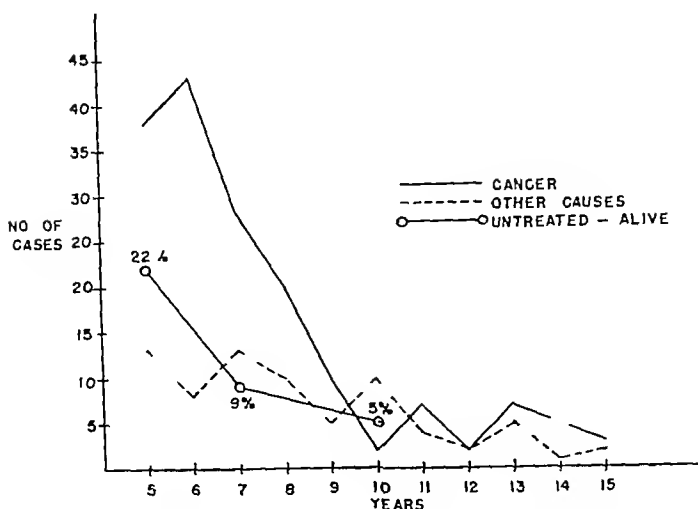


Fig 7 Deaths from cancer and other causes after 5 years, 238 cases

ment because of the presence of axillary metastases is therapeutic defeatism at its worst

In general terms, it seems evident that of every ten 5 year cures, not more than 6 are Stage A at the time of treatment, usually the other 4 are Stage C, and very occasional patients will survive 5 years or more without recurrence when the disease has involved the supraclavicular nodes. This is not to imply that all patients in the Stage C group should be regarded as candidates for radical mastectomy, for their therapeutic management demands the utmost nicety of clinical judgment, based on a number of factors beyond axillary involvement *per se*. In fact, there are criteria of operability within the Stage C group, and many cases in this series are examples of the failure properly to apply such criteria. The point, however, must be made, that almost 40 per cent of 5 year cures will accrue from the proper management of Stage C cases, and consistent therapeutic indolence in these cases will result in the loss of 4 of every possible ten 5 year cures.

Survival For the purposes of this study, a 5 year post-treatment period free from recurrence or metastasis has been used as a criterion of cure. There are certain forms of cancer with a predilection toward delayed recurrence so notable as to make the arbitrary 5 year period a poor gauge of therapeutic success. Basing his opinion upon a follow-up study of 167 cases, Bartlett concluded that "what happens after the fifth year is relatively unimportant," stating that only 1 patient died in the second 5 years. There is no small amount of evidence opposing this conception. Duccing reported a progressive decrease in survivors from 8

per cent at the end of 5 years to 2.2 per cent in the thirteenth year. From the fifth to the fourteenth years Lewis and Rienhoff followed 322 cases, the survivors decreasing from 30.9 per cent to 8.7 per cent, the maximum loss occurring by the ninth year. Matthews made a 10 year follow-up study and concluded that a patient surviving the first 5 years had a 62.5 per cent chance of living 10 years, and that deaths between 5 and 10 years were mainly from cancer rather than from intercurrent disease. Survivors in Perry's series of 653 cases decreased from 28 per cent at 5 years to 16 per cent at 14 years. In 419 cases of recurrence reported by Pfahler and Vastine, 7 per cent appeared more than 5 years after treatment. Breast cancer has recurred more than 30 years after treatment.

In this series, 1,207 cases were reported at a time when they had been free of disease for 6 or more years, and of these 869 were 6 to 10 year survivors, 264 were 10 to 15 year survivors, and 74 for more than 15 years. The curve of survival for the 869 cases of 6 to 10 year survivors is shown in Figure 6. In Figure 7, plotted against Daland's statistics of survival in 100 untreated patients, are the mortality curves for 238 cases in which the time and cause of death is known, for those dying both of recurrence and intercurrent disease. It is evident from these graphs that the number of reported survivors and the deaths from cancer, both in treated and untreated patients, level off after the ninth year. As a true gauge of end-results, therefore, the 5 year yardstick is best replaced by one in which curative achievements are measured on the basis of 9 or 10 year statistics.

SUMMARY

The records of 2,636 cases of mammary carcinoma, 1,511 5 year cures and 1,125 recurrent cases, have been reviewed. Comparative statistics are presented for the factors of age, childbearing, and the known duration of tumor. Collective data concerning the influence of heredity and lactation in the genesis of the disease are analyzed. The stage of disease at treatment and the survival period of the 5 year cures are separately presented.

CONCLUSIONS

The age of patients with mammary carcinoma does not have the prognostic significance with which it is commonly accredited. Excluding the cases of "inflammatory" carcinoma and those occurring in gravid and puerperal women, more common in the young, carcinoma of the breast at any early age merits as radical an approach with as much chance of cure as in older women. The best results are obtained in those patients who are 35 to 50 years of age, and the least favorable in the decade from 50 to 60.

There is evidence of an inherited susceptibility to cancer in approximately 20 per cent of this series, but among the relatives of those women having an hereditary background of cancer there is an excess of breast cancer at least 3 times greater than in the general population.

Nulliparae are more prone to develop cancer of the breast than women who have had children but once developed the prognosis is as good, or perhaps better for the nulliparous woman. The number of children borne by parous women has little or no influence on prognosis.

The most consistent apparent factor in the genesis of mammary cancer is the failure of the breast to perform its expected physiological function. A full period of lactation in childbearing women seems to offer a degree of protection against subsequent development of breast cancer.

Early treatment is of utmost importance in the cure of certain early lesions predestined otherwise to undergo rapid growth and early dissemination but in general end results are determined more by natural selection than by early treatment. Tumors of long duration in themselves are no contra indication to radical treatment, for 25 per cent of the 5 year cures here recorded were treated more than 1 year after recognition of the tumor.

To deny patients with otherwise operable neoplasms the chance of radical treatment because of the presence of axillary node metastases is to for the possible loss of 40 per cent of attainable 5 year cures. Criteria of operability exist within Stage C (II) cases, requiring consideration of combined methods of therapy.

The 5 year post treatment period as an arbitrary standard for the evaluation of therapeutic measures is inadequate for mammary carcinoma, and may well be replaced by a minimum 9 year period.

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CARCINOMA OF THE COLON AND RECTUM

A Study of Metastasis and Recurrences

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SUCCESS in the management of cancer of the colon and rectum customarily is evaluated in terms of survival rates over arbitrarily determined periods. Unfortunately, from the standpoint of the accuracy of such estimations, factors other than the cancer per se may act to curtail survival. A patient who has had his cancer completely extirpated may succumb to a pulmonary embolus a week later. As far as this individual patient is concerned, the treatment has been a failure although from a purely technical standpoint it was highly successful. However, had the patient not fallen victim to an unfortunate postoperative complication, the most important thing in determining his survival would have been the success attending the efforts of the surgeon to eradicate the cancer.

The present study concerns itself entirely with the technical side of the problem, namely, the ability of the surgeon to rid the patient of cancer. The influence of metastatic growths, their distribution in the body, the accuracy with which their presence can be detected by the surgeon, and, finally, the question of recurrence will likewise be considered.

MATERIAL

During the 5 year period beginning January 1, 1935, and ending December 31, 1939, 334 patients suffering from carcinoma of the colon and rectum died and were subjected to postmortem examination. The material employed in this study was obtained from the clinical records and protocols of the necropsies of these patients. Only cases of primary adenocarcinoma were considered. (This excluded 1 squamous cell epithelioma of the rectum, 1 sarcoma of the cecum, 1 case of Hodgkin's disease of the cecum, and 3 cases of carcinoma secondary to lesions elsewhere in the digestive system.) The distribution of the lesions was as follows: rectum, 83 cases, or 24.9 per cent, rectosigmoid, 41 cases, or 12.3 per cent, sigmoid, 77 cases, or 23.1 per cent, descending colon, 18 cases, or 5.4 per cent, splenic flexure, 10 cases, or

3.0 per cent, transverse colon, 13 cases, or 3.9 per cent, hepatic flexure, 11 cases, or 3.3 per cent, ascending colon, 24 cases, or 7.2 per cent, cecum, 29 cases, or 8.7 per cent, and 28 cases of multiple carcinomas, or 8.4 per cent. This distribution corresponds in general to the clinical distribution encountered at the Mayo Clinic and elsewhere (Lockhart-Mummery). The incidence of multiple carcinomas is higher than that reported by Bargen and Rankin or Schweiger and Bargen, owing to the fact that we included 8 cases of multiple polyposis with multiple malignant lesions and 5 cases in which two or more low grade polypoid malignant lesions were present.

FINDINGS

Metastasis. In order to determine the total incidence of metastatic growths and their distribution, the findings of the surgical pathologist at the time of operation (in those cases in which patients were subjected to surgical procedures), as well as those of the pathologist who made the postmortem examination, were consulted. Only those tissues showing microscopic as well as gross evidence of invasion were listed as sites of metastasis. It is to be remembered that these figures represent totals and are therefore higher than the surgical or postmortem figures alone. The findings appear in Table I.

The highest total incidence of metastasis occurred in cases of carcinoma of the transverse colon, followed by those of the rectosigmoid and splenic flexure, while the lowest incidence occurred in those of the hepatic flexure. When lesions of the transverse colon and multiple lesions are excluded, the incidence of metastasis is found to be 4.9 per cent higher from the left portion of the colon than from the right portion of the colon. The highest incidence of involvement of the regional lymph nodes occurred with carcinoma of the rectosigmoid, the second highest with carcinoma of the cecum, and the lowest with carcinoma of the splenic flexure. Carcinoma of the rectosigmoid likewise led in the incidence of hepatic metastasis. Metastasis to the lungs and pleura most commonly followed carcinoma of the rectum.

TABLE I.—INCIDENCE AND DISTRIBUTION OF METASTATIC GROWTHS

Site of primary tumor	Rectum	Recto-sigmoid	Sigmoid	Descending large colon	Splenic flexure	Trans- verse colon	Hepatic flexure	Ascending colon	Cecum	Multiple tumors	Total
Cases	83	47	77	25	19	5	17	84	39	36	264
Per cent without metastasis	44.6	56.3	37.7	44	30	83	54.5	47	47	47	5
Per cent with metastasis	55	40.7	62.3	55.5	70	17	45.5	57.3	52.3	53	95
Per cent of total Regional nodes	47	38.8	44	26.8	20	32.8	36	30	15	13.8	
Distant nodes	8	—	5	—	10	7.7	—	8.3	—	5	
Liver	7	37.7	26	11	20	5	27.3	20.8	13.8	17	
Lungs and pleura	16	7.3	6	8	—	—	9	12.3	10	30	
Other	13	64.4	26	6	30	32.8	17.5	27.5	31	30.7	16
Per cent showing local invasion	58.9	51.9	55	30	70	61.5	56.4	52.2	47.5	77.9	39

Peritoneal implants were found in 21.7 per cent of the cases. Other sites of metastasis included the jejunum or ileum, 6.6 per cent, omentum, 4.5 per cent, adrenals, 3.9 per cent, ovaries, 3.6 per cent, stomach, 3.0 per cent, pancreas and bladder, 2.4 per cent each, colon, 2.1 per cent, spleen, prostate, ureters, and diaphragm, 1.8 per cent each, mesentery, abdominal wall, and kidneys, 1.5 per cent each, duodenum, gall bladder or bile passages, bony skeleton, 1.2 per cent each, mesenteric, portal or hepatic veins, fallopian tubes, 0.9 per cent each, wound, uterus, vagina, iliac veins or vena cava, 0.6 per cent each, skin or subcutaneous tissue, sympathetic ganglia, mesenteric artery, rectum, myocardium, and brain, 0.3 per cent each. In most of the cases in which visceral metastasis occurred, involvement of the lymph nodes was noted, but this was not a constant finding.

In addition to metastatic implants, the tendency to local invasion is indicated in Table I. Invasion was said to have occurred when there was histological evidence of serosal involvement or penetration to adjacent tissues by the carcinomatous process. This is seen to have taken

place most commonly in cases of carcinoma of the splenic flexure and least commonly in cases of multiple tumors.

A more detailed investigation of metastatic growths in the liver was carried out to ascertain whether the site of the primary tumor had any influence on the location of the implants in the liver. It will be recalled that lesions of the left portion of the colon were more common than those of the right, and that the incidence of metastasis was slightly higher from the left portion of the colon than from the right. There were 74 cases in which metastatic growths occurred in the liver. In 5 cases—4 of which came from lesions of the rectum or sigmoid—these were confined to the left lobe. In 3 cases they were predominantly in the left lobe, in 48 cases there was diffuse involvement of both lobes. In 4 cases the right lobe was chiefly involved, and in 14 cases it was exclusively involved. In other words, involvement of the right lobe preponderated in 24.3 per cent of the cases, of the left lobe in 20.8 per cent.

Recognition of metastatic growths. In order to determine the degree of accuracy with which the surgeon was able to recognize the presence of

TABLE II.—EVIDENCE OF EXTENSION OF CARCINOMA IN GROUP OF CASES IN WHICH NO EXPLORATION WAS CARRIED OUT
(Postmortem findings)

Therapeutic class	Cases	Per cent of cases without metastasis	Per cent of cases with metastasis	Per cent of cases with regional nodes involved	Per cent of cases with hepatic metastases	Per cent of cases with other metastases	Per cent of cases with local invasion
No operation	18	—	33	—	50	54.5	33
Emergency operation	18	44	55.5	44	33	33	22
Follow-up or irradiation or both	—	44	55	33	44	44	—
Incidental postmortem finding	22	95	—	5	—	—	5
Total	58	57.4	55	40	30	32.4	16

TABLE III—CASES IN WHICH ABDOMINAL EXPLORATION WAS CARRIED OUT

Operative procedure	Cases	Findings	Per cent of cases in which no metastasis was found	Per cent of cases in which metastasis was found	Per cent of cases with regional nodes involved	Per cent of cases with hepatic metastasis	Per cent of cases with other metastasis	Per cent of cases with local invasion
Exploration only	13	Operation	30.8	69.2	0	53.8	38.5	0
		Necropsy	15.4	84.6	69.2	69.2	61.5	46.3
Palliative operation	38	Operation	26.3	73.7	23.7	42.1	42.1	68.4
		Necropsy	5.3	94.7	60.5	37.9	68.4	71.1
Preliminary operation	44	Operation	81.8	18.2	2.3	(4.5?)	11.4	(38.6?)
		Necropsy	47.7	52.3	34.1	11.4	27.3	36.4
Total	95	Operation	52.6	47.4	10.5	26.3	27.4	45.3
		Necropsy	26.3	73.7	40.5	37.9	48.4	51.6

metastatic growths at the time of operation, an analysis of the cases was made on the bases of the procedures to which each patient was subjected. The cases were divided into two main groups. The first consisted of 70 cases in which no exploration was carried out. This included 22 cases, 6.6 per cent of the total, in which no operation was performed, 18 cases, 5.4 per cent, in which emergency operations were performed because of obstruction or perforation of the bowel and in which exploration was not feasible, 9 cases, 2.7 per cent, in which treatment was given by fulguration or irradiation or both, and 21 cases, 6.3 per cent, in which the tumors were incidental findings at postmortem examination. The second group consisted of 264 cases in which opportunity was afforded for exploration of the abdominal cavity by the surgeon. This group included 13 cases, 3.9 per cent, in which exploration alone was carried out, 38 cases, 11.4 per cent, in which palliative¹ procedures were carried out, 44 cases, 13.2 per cent, in which preliminary operations—such as colostomy or ileocolostomy in anticipation of subsequent resection—were performed, and finally, 169 cases, 50.6 per cent, in which presumably curative operations—resections—were performed.

Since the cases in the first group afforded no opportunity for the surgical recognition of metastatic growths, the postmortem findings alone were presented in Table II, chiefly for comparison with the findings in the second group. As would be expected, the highest incidence of cancerous extension, by local invasion or by metastasis, occurred in the group of cases in which no operation was performed because of the debility of the patient or clinical evidence of widespread metas-

¹Operations were designated as palliative not only when, because of local extension or the presence of metastasis, no attempt was made to remove the tumor and decompression or short circuiting alone was established, but also when resections were carried out in the presence of obvious metastatic growths in the liver or extensions of the tumor which could not be removed.

tasis. Likewise, the lowest percentage occurred in the group of small and unsuspected early carcinomas which were incidental postmortem findings.

In the group of cases in which the opportunity for exploration was afforded, a comparison of the operative and postmortem findings in the cases in which exploratory, palliative, or preliminary operations were performed is presented in Table III. The surgeon's opinion regarding local invasion and all metastatic growths except those in the liver was credited only when borne out by the findings of the surgical pathologist. In the case of metastatic growths in the liver the surgeon's opinion was recorded regardless of confirmation, which was seldom practicable. The average length of survival after operation was 43.7 days after exploration, 66.3 days after palliative procedures, and 16.8 days after preliminary operations. Marked discrepancies are seen to exist in the incidence of involvement of the lymph nodes between the operative and postmortem findings. These can be explained by the fact that in comparatively few of the cases in this group were the regional nodes removed for examination by the surgical pathologist. The ability of the surgeon to detect metastatic growths in the liver was fairly accurate, as will be shown later. The discrepancy in the case of other metastatic growths is due to the fact that only those which lay within the peritoneal cavity could be detected readily. Local invasion is seen to have occurred in 71.1 per cent of the cases in which palliative procedures were performed and in only 5.3 per cent of these cases were there no metastatic growths. The high incidence of metastasis—52.3 per cent—in cases in which patients were subjected to preliminary operation is of interest, as it indicates that many of these cases would not have been suitable for resection had the patients survived.

TABLE IV—CASES IN WHICH CURATIVE RESECTIONS WERE PERFORMED

Survival after operation	Cases	Operative findings					Postmortem findings				
		Evidence of spread of tumor	Per cent of cases	Mode of spread to cases with extension			Per cent of cases in which no metastasis was found	Per cent of cases in which metastasis was found	Distribution of metastases		
				Local	Median	Other			Cases	Liver	Other
More than 30 days	28	No extension	21.4				53.6	42.7	25	16.7	25
		Extension	64	74	53.6	3	30	57	26	75	25
		Total	85				53.6	47	51	51	51
31 days or less	131	No extension	36				27	17.6	7.6	3	1
		Extension	61	66	66.4	30	65	55	55	55	55
		Total	97				71.8	36	63	58	56
Total	69	No extension	57.3				77.8	34	33	7.9	26
		Extension	42.7	64	65	43	61.3	57.7	57	55	56
		Total	154				67.8	47	63	58	56

In Table IV are seen the findings in those cases in which supposedly curative operations were performed. There were 169 such cases. These were divided into two groups, those in which death occurred within 3 weeks of operation—131 cases—and those in which survival exceeded 3 weeks—38 cases, in some of which the patients lived several years after operation. In the latter group of cases, the surgeon found no evidence of extension of the tumor beyond the confines of the bowel in 13 or 31.6 per cent, of the cases. In 7 or 58.3 per cent, of those in which no extension was found, no metastatic growths were found at necropsy. In the remaining 5 or 41.7 per cent, metastatic growths were found at necropsy involving the lymph nodes in 3 or 25.0 per cent, the liver in 2 or 6.7 per cent, and other regions in 3 cases, 25.0 per cent. Residual carcinoma was found in 2 cases, 16.7 per cent. In the 26 cases in which the surgeon found evidence of extension—local invasion in 30 cases, metastasis to nodes in 14, metastasis elsewhere in 6—no metastatic growths were found at post mortem examination in 13 cases, 50.0 per cent. Metastatic growths found in the 13 remaining cases were located in the lymph nodes in 7 cases, 53.8 per cent, the liver in 4, 30.8 per cent, and elsewhere in 2 or 15.4 per cent. Recurrent or residual cancer was noted in 3 cases, 23.1 per cent.

The most interesting group of cases from the standpoint of the study at hand is the group in which resection was carried out and death occurred within 3 weeks of the time of operation, as the result of postoperative complications, such as shock, hemorrhage, pneumonia, peritonitis, or pulmonary embolism. The findings in those cases

presumably should differ very little from the conditions left by the surgeon at the conclusion of the operation, at least in so far as the status of the tumor is concerned. In this group of 131 cases, the surgeon found no evidence of extension in 36 cases, 27.5 per cent. When these 36 cases came to necropsy no metastatic growths were found in 42 or 83.3 per cent. Of the 9 remaining cases, 17.6 per cent, the pathologist found metastatic growths in lymph nodes in 4 or 7.8 per cent, in the liver in 3, or 5.9 per cent, and elsewhere in 1 or 2.0 per cent. Residual carcinoma was found in 2 cases, 2.2 per cent. In the 80 cases, 61.1 per cent, in which the surgeon found evidence of extension—local invasion in 48 cases, metastasis to lymph nodes in 55 cases, and other metastasis in 8 cases—52, or 65.0 per cent, were free of metastatic growths at postmortem examination. In the 28 remaining cases, 35.0 per cent, metastatic growths were found in lymph nodes in 9 cases, 32.1 per cent, in the liver in 8 cases, 28.6 per cent, and elsewhere in 11 or 39.3 per cent. Residual carcinoma was detected in 5 cases, 6.3 per cent. Considering all cases in which resection was carried out, the surgeon found no extension in 37.3 per cent, of these 77.8 per cent were free of metastatic growths at necropsy. He found extension in 62.7 per cent and 6.3 per cent of these were free of metastatic growths at necropsy. Residual carcinoma was found in 7.1 per cent.

The responsibility of recognizing metastatic growths does not fall on the surgeon alone. Preliminary skeletal, certain hepatic metastatic growths, and many others often can be discovered by the clinician or roentgenologist and the patient

may be spared futile and unnecessary operations. On the surgical pathologist rests the duty of identifying involved lymph nodes and of confirming gross evidence of visceral metastasis. Next to the regional nodes, the liver is the site in which metastatic growths are found most frequently. Since biopsy of suspicious tissue in this organ is not practicable routinely, the discovery and recognition of carcinomatous implants fall to the surgeon. With what degree of aptitude the surgeon meets this responsibility, the following study indicates.

In the entire series of 334 cases, there were 260 in which adequate opportunity for exploration of the liver by the surgeon was afforded. In 224 of these he considered the liver to be free of metastatic growths, in 12 there were areas which he regarded with suspicion, and in 24 cases, he felt that metastatic growths definitely were present. Of those cases in which the surgeon thought the liver was not involved, postmortem examination revealed an uninvolved liver in 197 cases, or 87.9 per cent, and a carcinomatous liver in 27, or 12.1 per cent. In the cases in which the surgeon was in doubt, the pathologist found metastatic growths in 6, or 50.0 per cent and none in 6, or 50.0 per cent. In those cases in which the surgeon believed metastatic growths to be present, the pathologist confirmed the impression in 22, or 91.7 per cent, but did not confirm it in 2 cases, or 8.3 per cent.

Factors contributing to recurrence. The most common cause of so called recurrence, in the broad sense of the term, probably is the failure to remove some portion of the primary growth or some of its secondary colonies. It is questionable, but possible, that in some cases implants may occur by contamination during the process of extirpation. But a very common cause, which usually does not receive the attention it merits, is the presence in the remaining segments of the bowel of areas bearing malignant or potentially malignant growths which have been wholly unsuspected. In the group of 169 cases in which curative resection was carried out, independent cancers were found in the bowel at necropsy in 7 cases, or 4.1 per cent.

Although unanimous agreement is not yet forthcoming as to the relation of adenomatous polyps to carcinoma of the large bowel, there is little room for doubt that in many cases the rôle played by polyps is more than coincidental. This impression certainly was borne out by the present study. Adenomatous polyps were found in 114, or 34.1 per cent, of the 334 cases reviewed. In these 114 cases, definite malignant changes were recognized in the polyps of 16, or 14.0 per cent. The ade-

nomatous polyps occurred singly in 54 cases, multiple polyps were noted in 52 cases, diffuse polyposis coli existed in 8 cases. In 15 cases the polyps were confined to the rectum, in 20, to the sigmoid, in 8, to the descending colon, in 10, to the transverse colon, in 7, to the ascending colon, and in 10, to the cecum. In 39 cases they were distributed over several segments. In 5 cases their location was not noted.

For purposes of comparison a review was carried out of 100 consecutive postmortem examinations performed on adults who had died of diseases other than carcinoma of the large bowel. Their ages ranged from 22 to 80 years, with an average age of 54.7 years. Polyps were present in 16 cases, 16.0 per cent. Eight of these, 50.0 per cent, showed beginning cancerous changes.

The true importance of adenomatous polyps appears when one considers the group of cases in which death occurred within 3 weeks of resection. Any polyps found in this group of 131 cases in all probability were present at the time of operation. They were found at postmortem examination in 49 of these cases, or 37.4 per cent. In 7, or 14.3 per cent, malignant changes had occurred.

OBSERVATIONS

Extension of carcinoma of the colon and rectum may take place by local invasion, via the lymphatics or via the blood stream. Extension is the chief factor influencing operability. Local infiltration is the most common form and spread by the other routes is said to occur relatively late. The extent of spread by the respective routes varies with different portions of the colon. We found local invasion most common with lesions of the splenic flexure, a fact which probably accounts for the high mortality rate attending removal of growths in this region. Invasion occurred with 28.9 per cent of the rectal carcinomas. Bagen and Larson noted it in 109 of 447 cases of rectal carcinoma. Attachments most commonly result from inflammation but, in our series, only cases in which actual invasion of the tumor was demonstrated were included.

We found regional nodes involved in 47 per cent of our cases. There was no progressive segmental increase or decrease extending from one end of the colon to the other. Boyd stated that spread is slowest in the distal portion of the colon and danger of recurrence is greatest in the proximal portion because of the more abundant lymphatics associated with the absorptive function of the latter. Rankin (21), on the other hand, found metastatic growths most common in the distal portion of the colon, least common in the proximal

portion, and attributed this distribution to the protective influence exerted by the lymphatics. We found involvement of the regional lymph nodes most common with carcinoma of the recto-sigmoid—58.5 per cent—but almost as common with cecal lesions—55.2 per cent. Craig and MacCarty found the lymph nodes involved with 32 per cent of the carcinomas of the cecum, while McVay found involvement with 47 per cent of rectal carcinomas. These figures were based on operative specimens and, accordingly, are lower than ours. However, Gliehrst and David found 68 per cent nodal involvement in their painstaking study of specimens of carcinoma of the rectum removed at operation.

Examination of the regional lymph nodes at the time of operation is of great importance in establishing a prognosis. Many attempts have been made to discover factors influencing nodal involvement. Naturally the longer a growth has been present, the greater the likelihood of extension. Rankin and Broders found that the incidence of nodal involvement paralleled the grade of the tumor—based on histological evidence of differentiation. Bacon and Gilbert stated that invading types of lesions are most likely to metastasize and Hayen, in his study of 100 cases of colonic cancer, found metastasis least common with growths which protruded into the lumen of the bowel.

Visceral metastatic growths were most common in the liver, the lungs and pleura coming second. Such metastatic growths occurred most often from carcinoma of the rectum or recto-sigmoid in our series. This was in accord with the observations of Harding and Hankins, who also noted the tendency of rectal lesions to produce visceral metastasis. Involvement of such structures as the bladder, other segments of the alimentary canal, and the abdominal wall was usually by direct extension rather than true metastasis. Ovarian involvement was sometimes by direct extension, sometimes blood-borne, giving rise to a Krukenberg tumor. Visceral metastatic growths may be chiefly lymph-borne or blood-borne. It generally is stated that evidence of nodal involvement is the most reliable indication of the presence of visceral metastatic growths. Rankin and Broders found the incidence of visceral metastasis paralleling the grade of the primary lesion. Brown and Warren, however, expressed the belief that the most valuable index of all is evidence of vascular invasion, as determined by careful study of 3 regions of the primary tumor. They noted visceral metastasis with 41 per cent of 170 cases of rectal carcinoma. In many of these cases no evidence of nodal in-

volvement was found but in only 1 case did visceral metastasis occur in the absence of local intravascular invasion.

Our study of the distribution of metastatic growths in the liver was not particularly fruitful. Injection experiments by McDonald and Conner, and others have suggested that the right and left lobes of the liver are anatomically independent as regard to their blood supply and excretory ducts. Such work has given rise to the question of the existence of a dual portal current, blood from the superior mesenteric vein (jejunum, ileum, and right portion of the colon) passing mainly to the right lobe, and blood from the frenal vein (splenic, left portion of the colon, rectum, and spleen) passing to the left. Although metastatic growths were most commonly diffuse, regardless of the site of the primary lesion, when there was a preponderance, it occurred more than twice as often in the right lobe as in the left, although lesions of the left portion of the colon and rectum were far more common than those of the right portion of the colon. This discrepancy could not be accounted for by a difference in the relative weights of the two lobes, which it is said rarely exceeds 50 grams.

In considering the problem of ridding the patient of his disease, only the group of 69 cases in which resection was carried out need be reviewed. In only 37.3 per cent of these cases was there no evidence of extension at the time of operation. Lymph nodes were involved in 40.8 per cent, involvement of overlying peritoneum or adjacent tissues had occurred in 40.8 per cent, and other metastatic growths were found in 8.8 per cent; 65.1 per cent, 64.2 per cent, and 3.8 per cent, respectively, of the cases which showed extension. In spite of this comparatively high incidence of extension, no metastatic growths were found at postmortem examination in 67.5 per cent and recurrent or residual carcinoma in only 7.1 per cent. In the group of 13 cases in which survival was 3 weeks or less and in which conditions presumably differed little from those at the completion of operation, it is found that, when no extension was noted at operation, metastatic growth could be discovered in only 17.6 per cent at postmortem examination and residual carcinoma in only 3.9 per cent. Furthermore, of the cases in which extension was noted at operation, only 35 per cent showed metastatic growths at necropsy and 6.3 per cent residual cancer. Obviously minute undiscovered metastatic growths may have remained, but the fact that gross evidence of cancer remaining anywhere in the body was absent in so high a proportion of cases after opera-

tion, even though extension was known to have occurred, reflects considerable credit on the efforts of the surgeon. In the group in which survival exceeded 3 weeks, sometimes by several years, an increase of 19.2 per cent in the incidence of metastatic growths was found at necropsy, distant metastatic growths which were beyond the scope of surgical intervention showing the greatest relative increase. Residual cancer increased 7.9 per cent but recurrences or new cancers probably contributed to this rise.

The foregoing figures and those of the other groups in which procedures other than resection were carried out, likewise furnish a fairly good index of the accuracy with which metastatic growths could be detected at operation. The recognition of metastatic growths is the determining factor in deciding whether an operation is to be an exploration alone or a palliative one, or whether resection is to be attempted, and if the latter, how much tissue can and must be removed. The surgeon overlooked metastatic growths in the liver in only 12.1 per cent of cases. Many of these growths were small and were discovered a long interval after surgical exploration. When suspicious areas were noted at operation, necropsy showed 50 per cent of them to be malignant, and finally, when the surgeon designated the liver as involved, he was correct 91.7 per cent of the time. Lesions in the liver which were potential sources of confusion to the surgeon were revealed at necropsy to include adenomas of the bile ducts, cysts, hemangiomas, tubercles, infarcts, and cirrhosis.

The importance of the presence of additional, independent lesions of the bowel in the development of recurrences has been shown by the findings at necropsy of additional cancers in 7 cases and cancerous polyps in 10 cases in the group in which resection was performed. The rôle of adenomatous polyps may be controversial but their presence in 34.1 per cent of all the cases of carcinoma of the colon and rectum in this study, in contrast to 16.0 per cent incidence in a group of patients of similar age who died from other causes, is suggestive, to say the least. Adenomatous polyps were left after operation in 34.3 per cent of the group in which resection was performed, the incidence of malignant polyps and frank secondary carcinomas being slightly higher in the group of cases in which the survivals were longer. The 50 per cent incidence of malignant changes in the polyps of the control group may seem incongruous at first sight until one recalls that the polyps in the series under consideration were associated with carcinomas in 100 per cent and, when one

speaks of malignant changes in 17.2 per cent of the cases in which polyps were present, one is speaking of polyps still left behind after resection of a full blown cancer.

Just as senile hyperplastic changes develop in the epidermis with advancing age, hyperplastic tendencies develop in the intestinal mucosa. Bagen stated that some form of polypoid hyperplasia of the mucosa is present in 50 per cent of persons more than 30 years of age. The frequency with which polyps occur is difficult to estimate. Clinically, Buie has found them in 1 of every 35 patients undergoing proctoscopic examinations, polypoid lesions are seen in 1.8 per cent of the colons examined roentgenologically at the Mayo Clinic. Pathologically, Stewart has shown that the reported incidence of polyps varies with the care with which they are sought. He found them associated with 29.6 per cent of the cancers of the colon that he studied. Susman found polyps in 6 per cent of 1,100 consecutive postmortem examinations. Only 7 per cent of these polyps occurred in persons less than 40 years of age, although 40 per cent of his cases fell into this age group. Fifteen of his 66 patients having polyps had cancer of the colon and, among 34 cases of cancer of the colon, polyps were present in 15, the peak of incidence of both lesions falling between the ages of 50 and 70 years.

The most suggestive evidence of the relation of adenomatous polyps to cancer is found in the familial cases, although these tend to occur in younger age groups. Rankin (21) stated that cancer of the colon develops in 50 per cent of these cases. FitzGibbon and Rankin, David, and others, by careful pathological studies, have traced the development of cancer from polyps. In examination of patients who had refused to submit to fulguration, Buie has seen carcinoma at the site previously occupied by polyps. Lockhart-Mummery and Dukes described mucosal irregularity adjacent to cancers of the colon, localized areas of epithelial hyperplasia extending several inches away from the growth. They expressed the belief that adenomas represent a more advanced stage of this hyperplasia, which may develop into carcinoma in certain cases. The opinion was also expressed that after carcinoma has developed, hyperplasia and benign tumors regress.

The importance of the submucosal lymphoid aggregations in the production of these epithelial changes has been emphasized by Coffey and Bagen. More recently, an interesting investigation and review of the topic have been reported by Bagen, Cromar, and Dixon.

The origin of polyps sometimes is inflammatory in association with such conditions as chronic ulcerative colitis, tuberculous enteritis, old strictures of the bowel and so forth. Although these often are not true adenomatous polyps, occasionally they are. In 6 of our cases carcinoma of the large bowel developed in association with chronic ulcerative colitis. The question has even been raised whether the polyps occurring in connection with carcinoma of the bowel may not be the result of the irritating influence exerted by the presence of an ulcerating cancer. But hyperplastic and polypoid changes are more common around small, early carcinomas than around large, late lesions, according to Lockhart Mummery and Duke. Yocom has emphasized the primary importance of irritation and inflammation in the development of polyps and carcinoma. In accord with the old views of Virchow and of Verne

Whether one believes that all cancers of the colon arise from polyps and that all polyps are potentially malignant, or not, there is no denying that accessory growths often are responsible for so called recurrences. The practical importance of this is apparent. Whenever a carcinoma of the colon is encountered, the presence of another malignant or potentially malignant lesion should be suspected and carefully ruled out. Having discovered a carcinoma by proctoscopic examination, the clinician should not settle back in the happy assurance of having fulfilled his obligation to the patient. In the absence of obstruction recent genologic study of the remainder of the colon should be carried out to eliminate the possible presence of another lesion. The entire colon should be explored carefully by the surgeon at the time of operation. All malignant lesions should be removed. Benign lesions should be removed fulgurated, or kept under faithful observation. In all cases in which resection is performed, follow-up studies should be carried out at periodic intervals. There is considerable clinical and experimental evidence to support the hypothesis that the presence of a cancer inhibits the development of a second cancer. When the primary lesion is removed, this restraining influence disappears and another potentially malignant region may undergo carcinomatous degeneration.

It is beyond the scope of this paper to discuss the influences at work in the production of hyperplastic or malignant changes or changes which normally hold cell growth and regenerative processes in check. Yet the subject is not so controversial but that certain of its connotations should be borne in mind by all who are called on to diagnose and treat carcinoma of the colon and

rectum. Only by thorough and painstaking investigations of each case will avoidable "recurrences," due to accessory lesions, be prevented.

SUMMARY

A clinicopathological study of 334 cases of carcinoma of the colon and rectum has been presented. Regional or distant metastasis occurred in 60.5 per cent of the cases and local invasion in 39.5 per cent. Among cases in which there was hepatic metastasis, no correlation could be found between the site of the primary tumor and the site of involvement in the liver.

The ability of the surgeon to detect metastasis at the time of operation was found to be good. Among cases in which death occurred shortly after resection no metastasis was found at necropsy in 82.4 per cent of those in which none was found at operation. The success of extirpation was revealed in this same group of cases, 65 per cent of those in which there was metastasis at operation being free of it at necropsy. Residual cancer was found in only 5.3 per cent of the cases in which death occurred shortly after resection. In those cases in which the surgeon believed metastatic growth to be present in the liver, the pathologist confirmed the impression in 91.7 per cent.

Independent growths are felt to be responsible for many "recurrences." Polyps were present in 34.1 per cent of the cases in this entire series, in contrast to 16.0 per cent of a control series consisting of patients without cancer of the bowel. In 14.0 per cent of the cases in which polyps occurred, malignant changes were found in the polyps. Multiple carcinomas were found in 8.4 per cent of the cases. Among cases in which resection was carried out, additional independent cancers were found at necropsy in 4.1 per cent.

Whenever a carcinoma is found in any portion of the colon or rectum, the presence of a second carcinoma must be carefully ruled out. After operation, the malignant potentialities of the remaining mucous membrane should be borne in mind and careful follow-up studies carried out.

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AN ARTIFICIAL ILEOCECAL VALVE

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IT has been established that the normal ileocecal valve serves two important physiological functions: namely, (1) to avoid too rapid emptying of ileal contents into the cecum, thereby permitting maximal digestion and absorption of food products, and (2) to prevent a reflux of fluids laden with great numbers of bacteria and with toxic end products from putrefaction, into the rapidly absorbing ileum. Besides this protective mechanism furnished by the valve there is, of course, the relatively great abundance of lymphoid tissue, in the form of "Peyer's patches," in the walls of the terminal segments of the ileum. These, as Huntington concluded from his investigations, protect the body from invasion by microorganisms in that stretch of the gastrointestinal tube. It is particularly in the cecum, where the presence of a liquid nutrient medium represented by the fluid intestinal content or feces is conducive to luxuriant bacterial growth that the danger of bacterial invasion is great. That the strain on the protective mechanism of the junction of small and large intestine is considerable is indicated by the frequency with which that lymphoid tissue breaks down with resultant peritonitis and often death.

According to Alvarez and Rankin, the mucosa of the colon, on the other hand, appears to be a very efficient barrier to the passage of toxins into circulation. One of the features that is said to protect the body from auto-intoxication is the dryness of the feces in the middle and descending portions of the colon. About the only place in which absorption of bacteria and their toxins and the end products of protein putrefaction are likely to occur is in the first part of the colon where the fecal material is sufficiently liquid, although toxins that are absorbed here are believed to be slightly altered by the mucosa of the colon and by the liver. Rankin states that "more dangerous and more deleterious to health than the passage of chemical substances is probably the passage of bacteria from the cecum and terminal portion of the ileum into the lymph passages and nodes of the mesentery."

A number of investigators have shown that bacteria are constantly getting through the wall of the bowel and there is evidence that at times,

as may occur after purgation or after intestinal upsets, this grade of infection of the lymph nodes or of the blood stream is severe enough to injure health. Excepting perhaps the mouth and the pharynx, the ileocecal area of the gastrointestinal tract, for the reasons stated, is most vulnerable and most exposed to attack by bacteria and their toxins.

On the basis of the incompetence of the ileocecal valve seen by x-ray examination in some patients with gastrointestinal complaints, the opinions expressed by many roentgenologists differ greatly regarding its significance. Hunt declares unequivocally that the ileocecal sphincter does not prevent regurgitation into the ileum. He has seen bismuth suspension pass into the ileum when run into the colon at a pressure as low as 1 foot of water. "There can be no doubt," he says, "that the function of the sphincter is, as Keith suggested, to prevent the contents of the ileum from passing too rapidly into the cecum." Barclay and others are of the opinion that the competence or the incompetence of the ileocecal valve is of no significance in diagnosis. Singer and H. Itzknecht observed incompetence in numerous cases of obstipation, and this occurred whether the cecum was filled or not. Carmen declares that incompetence of the ileocecal valve is of all degrees, ranging from a trivial backflow to an extensive filling of the lower ileum.

Of those who regard incompetency of the ileocecal valve as a significant factor in diagnosis are Case, Dietlen, Ivy, Carmen, and others. Dietlen states that while the ileocecal valve is incompetent in infants, it is normally competent in children and adults. Case has observed a reflux of ingested bismuth suspension from the colon to the ileum in many cases and believes that valvular incompetency is a significant abnormality and that it is a common cause of fecal stases. Carmen doubts that an enema, put into the bowel under unphysiological conditions which necessitate at least a slight degree of hydrostatic pressure, would be a fair test of the physiological competence of the valve. A regurgitation of ingested material into the ileum after once passing the ileocecal valve would, he claims, theoretically have much greater import. Whether incompetency of the ileocecal valve indicates an unimportant perversion or a faulty of function or is significant of

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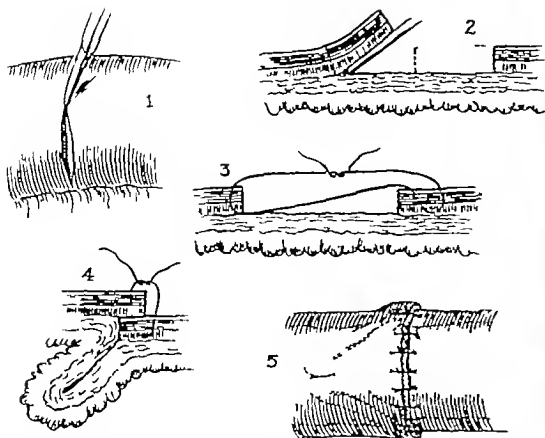


Fig 1 1, Surface view, showing circumferential incision passing through the serous and muscular coats 2, Longitudinal section, showing the manner of elevating the flaps by blunt dissection, and the removal of the flaps to denude the intestinal segment. It should be noted that the instrument should pass through the submucosa as the line of cleavage 3, Passing of the stitch from the left edge of the denuded stretch over and through the right edge 4, 5, Drawing together of the sutures, with approximation and overlapping of the edges, and the invagination of the circular mucosal fold

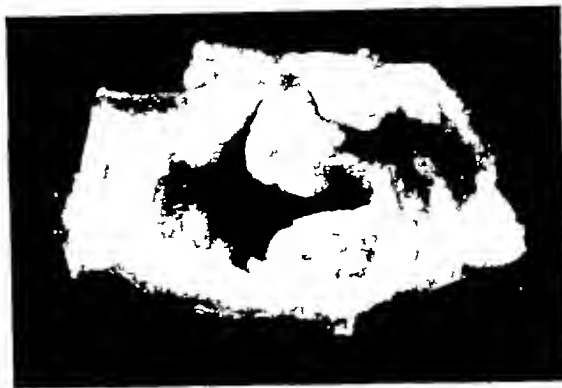


Fig 2 Photograph of a longitudinal section of the gross specimen of the ileum containing the newly formed valve Slightly magnified

struct the normal anatomy, that is, he makes no attempt to reproduce a valve-like structure somewhere in the anastomosis

In the experiments of reproducing intestinal valves that should resemble the true ileocecal valve, dogs were used In addition to developing a technique for the formation of such a valve, I made a preliminary comparative study of the bacterial flora in the small intestine of the animals in which ileocolostomies were made with and without the incorporation of the newly constructed valve

OPERATIVE PROCEDURE

The method described in the following furnishes an ileocolic valve of excellent function, and the experimental cases in which it was introduced and subjected to trial have proved its competency throughout the period of observation In the process of its reconstruction, the valve can be made to project in a given direction, thereby permitting the passage of food substances to take place in that direction only and preventing a reflux in the opposite direction Before the anastomosis of the small and the large bowel is undertaken, the valve-like structure is first formed in the distal segment of the ileum approximately 15 to 20 centimeters from the chosen site of ileocolostomy By constructing the valve first, that is, before opening the bowel, the operator works in a strictly aseptic field

Figure 1, 1, illustrates a piece of small intestine in which a circumferential seromuscular incision is carefully made down to and through the submucosa almost up to the exterior surface of the mucosa With the blunt end of the scalpel, as shown in Figure 1, 2, the severed seromuscular layer is raised by dissection from both sides of the

serious pathology, with possibilities in the way of differential diagnosis, remains to be determined Some surgeons, notably Kellogg, considered ileocecal incompetence of sufficient significance to devise methods for its repair

Physiological studies of the functions of the ileocecal valve have been carried out by such investigators as Ivy, Wright, Starling, Hartridge and Evans, and others Their conclusions are quite in accord with one another, namely, that the function of the ileocolic sphincter is to retain chyme in the ileum until digestion and absorption are completed and to prevent regurgitation of fecal material into the ileum

With the belief that the surgeon does not give sufficient consideration to the physiological significance of an ileocecal valve when he chooses to do reconstructive surgery of the bowel, such as ileocolostomy and ileosigmoidostomy, I turned to the development of a technique for the utilization of a segment of the intestine in the formation of a valve resembling the ileocecal valve grossly histologically, and physiologically

In surgical procedures in which there is need of doing "short-circuiting" operations, such as ileocolostomy and ileosigmoidostomy, the operator after severing the distal portion of the ileum and anastomosing the proximal end to the transverse or the sigmoid colon, invariably fails to recon-

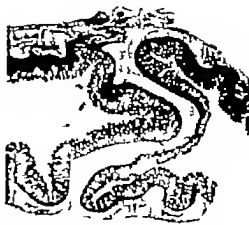
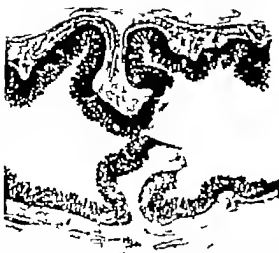


Fig. 5. Photomicrographs of stained longitudinal section through the segment of ileum containing the newly formed valve. $\times 50$. a, Section passed through the center or apex of the valve; the absence of the mucosa from one part of

its margin is an artefact. b, Section passed more tangentially through the valve. In both cases the muscular layer is seen to extend past the valve into the normal abdominal fold representing the ileocecal junction.

incision. In the dog, each raised flap needs to be about 1.5 centimeters in extent; yet, in every case the extent of the flap depended upon the diameter of the small bowel selected. The flaps are then cut off at their base, as indicated in Figure 1, so that a section of bowel about 3 centimeters in length is now denuded or lacking its seromuscular coat. Knowing the direction in which the protrusion of the valve must point, that is, toward the lumen of the large bowel, the operator proceeds to invaginate the denuded mucosa into the lumen. To achieve the correct pointing of the valvular fold away toward the left, as portrayed in Figure 1, 4 and 5, the interrupted suture employed is placed through the left seromuscular edge (Fig. 1, 3). Then the suture is continued through the right seromuscular layer but approximately 7 to 10 millimeters from its free edge (Fig. 1, 3). The suture is now drawn together and tied (Fig. 1, 4 and 5) while an assistant helps to keep the mucosa invaginated. Several interrupted sutures of black silk, or of chromic catgut (No. 000) are successively placed until the edges of the entire intestinal circumference (Fig. 5) are brought together in such a way that the left edge overlaps the right. This brings about maximum amount of invagination of the circular mucosal fold, which now serves as the valve (Fig. 5) by permitting the intestinal contents to pass toward the colon but preventing their reflux by virtue of its ability to constrict and approximate itself to the point of complete closure.

Because of the frequent postoperative distention (Jones) of the ileum near the point of anastomosis, the chosen site of the valve is safely beyond and should therefore not become incompetent as a result of that distention. Moreover, the ample distance between the anastomosis and the position of the valve provides for a better blood supply on both its proximal and its distal sides. From the photographs (Figs. 2 and 3, a and b) of longitudinal sections of the bowel containing the newly constructed valve it is seen that the latter is a projecting fold with a central core of muscle and submucosa covered on both sides by mucosa.

The mechanical effectiveness and strength of such newly constructed valves were tested in some of the experimental dogs after sufficient time had elapsed to permit healing of the intestinal wounds. Clamps were placed on the bowel some distance (15 cm.) from the valve both proximal and distal to it. Then water was injected under pressure into the distal segment until this became distended. A considerable distention and back pressure was necessary before the valve became incompetent and allowed the water to rush into the collapsed proximal segment of the bowel.

In addition to such experiments, fluoroscopic studies were made on exteriorized bowel segments containing the anastomosis. By means of a Luer syringe, a barium sulfate solution was injected into the colon and observed as it passed into the

loop of anastomosed ileum containing the artificial ileocecal valve. The distal loop of the ileum became markedly distended before the barium was actually seen streaking into the loop of the ileum proximal to the valve. Apparently, the continued distention and the increasing back pressure of the barium rendered the valve incompetent.

Films were taken to illustrate further the efficiency and mechanism by which the return flow of colonic content is prevented from passing beyond the selected site of the artificial ileocecal valve.

In Figure 4, a, an exteriorized segment of colon from an experimental animal was clamped off on both sides of the ileocolic anastomosis and filled with barium sulfate solution. The site of the ileocolic union is seen to be distended, which indicates that the actual point of anastomosis offers no barrier to the reflux of the colonic material into the ileum. On the other hand, the site and actual outline of the artificial ileocecal valve is clearly made out in Figure 4, b. The shadow cast by the barium is bifurcated at the site of the valve, and this contour of shadow results from the fact that the valve is teat-like or cone-like with its apex pointing toward the ileocolic junction. As the barium backed into the space between the protrusion of the valve and the surrounding wall of the bowel, its pressure probably contributed to the closure of that orifice. In the same figure some barium is seen streaking through the valvular aperture.

BACTERIOLOGICAL STUDY

In consideration of the effect of such a valve on the bacterial flora in the intestinal canal proximal to it, a preliminary bacteriological study was undertaken on a group of dogs subjected to ordinary ileocolostomy and on another group subjected to valvular ileocolostomy of the kind just described. Though the number of animals used thus far is too small to permit final conclusions, the results obtained appear to be significant and sufficiently encouraging to urge a continuance of the investigation.

On culture of the material obtained from the dog's ileum, both on Endo's and plain media, *Bacillus coli* was found to be the predominant organism. In several instances *Streptococcus fecalis* was also isolated, but in association with *Bacillus coli* and in numbers far less than the latter. Therefore, the only method available for a comparative study of the bacterial flora in the two groups of animals was a quantitative determination, that is, a count of the number of pure colonies of *Bacillus coli* isolated.



Fig 4 a, An exteriorized segment of colon clamped off on both sides of the ileocolic anastomosis and filled with barium. The actual site of anastomosis offers no barrier to the reflux of the colonic material into the ileum. b, A shadow cast by barium that is bifurcated at the site of the valve, this shadow represents the true contour and direction of the teat like valve.

To obtain the bacteria, 5 cubic centimeters of warm sterile water in a Luer syringe, fitted with a Wassermann needle, was injected into the lumen of the ileum and withdrawn again into the syringe. Samples were taken from 6 consecutive levels, at 30 centimeter (1 foot) intervals, oral of the valve. The samples thus obtained were collected separately in sterile test tubes and cultured the same day.

Six such sample specimens were cultured on both Endo's and plain media, and after 24 hours of incubation the quantitative estimations were made directly from the culture dishes as follows: 1+ was taken to express a growth consisting of from 1 to 25 colonies of *Bacillus coli*, 2+ from 25 to 50 colonies, 3+ from 50 to 100 colonies, or twice the number of the preceding, while 4+ expresses a growth so "heavy" that an accurate count could not be made.

To study the effect of the introduction of the operative procedure, whether it be an ordinary

TABLE I—THE EFFECT OF ORDINARY ILEOCOLOSTOMY ON THE BACTERIAL FLORA IN THE ILEUM OF THE DOG

Dog No.	Operative steps	Days post-operative	Culture medium	Bacterial growth from the samples of intestinal material taken at the indicated distances west of the ileocolic valve						
				Organism	30 cm or ft	60 cm or ft	90 cm or 3 ft	30 cm or ft	30 cm or 3 ft	Place
	1st step		Eagle Plasma	B. coli Strep. fecalis	+	+	+	+	+	+
	Second step	days	Eagle Plasma	B. coli coli	+	+	+	+	+	+
	First step		Eagle Plasma	B. coli coli	+	+	+	+	+	+
	Second step	day	Eagle Plasma	B. coli Strep. fecalis	+	+	+	+	+	+
	First step		Eagle Plasma	coli Strep. fecalis	+	+	+	+	No growth	
	Second step	day	Eagle Plasma	coli B. coli	+	+	+	+	+	No growth
	First step		Eagle Plasma	coli Strep. fecalis	+	+	+	+	+	No growth
	Second step	day	Eagle Plasma	B. coli Strep. fecalis	+	+	+	+	+	No growth
	First step		Eagle Plasma	B. coli coli	+	+	+	+	+	No growth
	Second step	14 days	Eagle's Plasma	B. coli B. coli	+	+	+	+	+	+
	First step		Eagle Plasma	B. coli Strep. fecalis	+	+	+	+	+	+
	Second step	43 days	Eagle Plasma	B. coli	+	+	+	+	No growth	No growth
	First step		Eagle Plasma	coli	No growth	No growth	No growth	No growth	No growth	No growth
	Second step	8 days	Eagle Plasma	B. coli	No growth	No growth	+	Strep. fecalis	Strep. fecalis	No growth

First or preoperative step: Obtainment of the bacteria as described in the text.

Operation: Ileocolostomy.

Second or postoperative step: Resampling the animal some time later for the withdrawal of bacteria as described.

ileocolostomy or a valvula ileocolostomy each dog was examined bacteriologically by the method indicated both before and a certain period after the operation. In this way comparative data were obtained for each individual dog, as set forth in Tables I and II. To interpret the results properly the data as a group must be compared, but the preoperative and postoperative states of each dog should be considered as the significant points, since any dog normally may differ from the next in his bacterial flora especially quantitatively. The incorporation of the results from the different animals in the same table is simply a matter of convenience.

By referring to Table I dog 1 it is seen that 13 days after an ordinary ileocolostomy was performed the bacterial count rose to more than twice the number of *Bacillus coli* present prior to the surgical operation. Similarly dog 2 also shows a marked increase in its bacterial count 9 days fol-

lowing surgery. At 150 centimeters (5 ft.) it reveals *Streptococcus fecalis* in a considerable number which apparently did not exist there before the anastomosis was made. In dog 3, no particular changes are noticed until the 120 centimeter (4 ft.) level in the ileum is reached. Here after 14 days, the bacterial count rises from 2+ to 3+ thus indicating an increase of approximately two times the number of bacteria originally present. At a point 50 centimeters (5 ft.) it reveals *Streptococcus fecalis* in a considerable number which apparently did not exist there before the anastomosis was made. In dog 3 no particular changes are noticed until the 20 centimeter (4 ft.) level in the ileum is reached. Here after 4 days, the bacterial count rises from + to 3+ indicating an increase of approximately two times the number of bacteria originally present. At a point 150 centimeters (5 ft.) in the ileal segment of the same animal, *Bacillus coli* and *Streptococcus fecalis* ap-

TABLE II—THE EFFECT OF VALVULAR ILEOCELOSTOMY ON THE BACTERIAL FLORA IN THE ILEUM OF THE DOG

Dog No	Operative steps	Days post operative	Culture medium	Bacterial growth from the samples of intestinal material taken at the indicated distances oral of the ileocecal valve						
				Organism	30 cm or 1 ft	60 cm or 1 ft	90 cm or 1 ft	120 cm or 4 ft	150 cm or 5 ft	180 cm or 6 ft
1	First step		Endo Plain	B coli B coli	1+	1+	1+	1+	1+	No growth
	Second step	14	Endo s Plain	B coli B coli	1+	1+	1+	1+	3+	No growth
2	First step		Endo s Plain	B coli Strep fecalis	1+ 1+	1+	1+	1+	1+	1+
	Second step	14	Endo s Plain	B coli B coli	1+	1+	+	2+	1+	No growth
3	First step		Endo s Plain	B coli Strep fecalis	1+ 3+	4+	3+	1+	2+	No growth
	Second step	14	Endo s Plain	B coli B coli	1+	3+	2+	2+	2+	No growth
4	First step		Endo s Plain	B coli B coli	2+	2+	No growth			
	Second step	9	Endo s Plain	B coli B coli	1+	1+	No growth			
5	First step		Endo s Plain	B coli B coli	4+	4+	3+	1+	+	2+
	Second step	14	Endo s Plain	B coli B coli	4+	1+	3+	2+	2+	No growth
6	First step		Endo s Plain	B coli B coli	1+	1+	1+	1+	No growth	
	Second step	5 mo	Endo s Plain	B coli Strep fecalis	2+ 1+	1+	No growth		1+	No growth
7	First step		Endo s Plain	B coli	4+	4+	No growth			
	Second step	27	Endo s Plain	B coli	1+	2+	1+	No growth		
8	First step		Endo s Plain	B coli	4+	4+	4+	4+	4+	4+
	Second step	60	Endo s Plain	B coli	4+	1+	2+	No growth		

First or preoperative step: Obtaining the bacteria as described in text

Operation: Valvular ileocolostomy as described

Second or postoperative step: Reopening the animal sometime later for the withdrawal of bacteria as described

pear, both of which were absent there before the operation. Dogs 4 and 5 exhibit only a comparatively slight increase in the postoperative bacterial count. That a shift of the colonic organisms to abnormally higher levels in the ileum occurs after elimination of the natural ileocecal valve by the usual "short-circuiting" operation is indicated by animals 3 and 5.

Table II embodies the results of the bacteriological examination after the introduction of a valve with the ileocolostomy; this series of dogs shows in general that the bacterial flora either remains unchanged from the normal, or even is reduced, which indicates a favorable effect of the inclusion of the valve. In comparison with the preoperative state, dog 1, for instance, reveals no appreciable bacterial change, 14 days after the

operation, in the entire stretch of ileum examined. Dogs 2, 3, 4, 5, and 6 manifest a variable reduction in bacterial counts after operation. Even a small shift of the *Bacillus coli* organism toward the colon is seen in dogs 2 and 5, an observation which is as favorable a point for the valvular ileocolostomy as the shift in the opposite direction is an unfavorable point for the ordinary ileocolostomy.

In addition to the bacteriological study, general observations of the condition of the animals—appearance, frequency of defecation, type of stool, etc.—after the operations furnished some measure of the relative effects of the two types of ileocolostomy. Of 14 dogs, which were subjected to the ordinary type of ileocolostomy, almost all of them had increased number of bowel move-

ments, liquid stools, and as a consequence the appearance and symptoms of dehydration. On the other hand the dogs in which a newly constructed valve was added to the ileocolostomy showed an appearance and conditions of defecation which deviated little from the normal state.

SUMMARY AND CONCLUSION

The present paper describes a surgical method which utilizes a segment of the intestine for the formation of an artificial ileocecal valve that resembles the normal ileocecal valve grossly, histologically and physiologically. By the addition of such a valve to an ileocolostomy the attempt is made to reconstruct the normal anatomy as closely as possible.

A preliminary bacteriological study revealed that the bacterial flora in the ileum of a dog after a valvular ileocolostomy was performed remained essentially unchanged, and in some instances even showed a smaller number of organisms. This result is in contrast to the findings in cases of ordinary ileocolostomy in which greater numbers of organisms were isolated, and at intestinal levels higher than occurred normally.

Comparison of the general state of the animals after ordinary ileocolostomy with that of animals after valvular ileocolostomy also furnishes evidence that the second or new procedure leaves the animal in a better condition physiologically than the first.

The conclusion is warranted that the introduction of a valve of this kind in ileocolostomies in man can be recommended in surgery.

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TREATMENT OF OBSTRUCTIVE HYDROCEPHALUS IN ADULTS

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SURGICAL procedures for the relief of hydrocephalus fall into three principal categories. They are carried out for (1) removal of the cause of obstruction, (2) reduction of the output of cerebrospinal fluid, (3) establishment of a new channel to permit the spinal fluid to escape from the ventricular system and reach the areas of absorption in the subarachnoid space. Methods of removing lesions which block the third and fourth ventricles or compress the sylvian aqueduct are already well known and therefore do not come under the subject discussed in this report. Treatment of the communicating type of hydrocephalus also constitutes a special problem quite separate from the conditions included herein. The type of hydrocephalus which we wish to discuss is produced by inoperable tumors in the region of the third and fourth ventricles or the intervening aqueduct and the still rarer benign occlusions of the aqueduct of Sylvius. Patients with this condition suffer from severe headaches and vomiting, progressive loss of vision from papilledema, and terminal failure of the intracranial circulation and respiratory paralysis.

In the past, treatment of hydrocephalus caused by inoperable tumors has been discouraging, but in recent years two methods of establishing free and lasting drainage of the ventricular system into the subarachnoid space have been described. Five years ago Stookey and Scarff advocated opening the anterior and posterior walls of the third ventricle and permitting the obstructed cerebrospinal fluid to escape into the large suprachiasmatic and interpeduncular cisterns. This operation had already been described by Dandy (3), but his exposure usually necessitated cutting one optic nerve and his results in young children have been unsatisfactory as we shall note. It was also performed by Cushing in at least one patient and the operation was illustrated in a sketch. The results are not mentioned, but the Peter Bent Brigham Hospital records state that 2 years later the patient remained relieved of her obstructive hydrocephalus and had recovered nearly normal vision. In 1939 Torkildsen described an alternative method

of shortcircuiting the flow of spinal fluid from one of the lateral ventricles into the cisterna magna by means of a rubber catheter. After the standard suboccipital craniectomy and the discovery of an inoperable obstructing lesion, this procedure is carried out by placing one end of a catheter in the posterior horn of one of the lateral ventricles through an occipital burr hole and then passing the other under the galea and scalp so that it can be fixed in the cisterna magna.

Either method is capable of establishing lasting drainage. Each operation has certain advantages, and both are far superior to older methods, which have never been really satisfactory. These procedures and the reasons for their failure should be briefly mentioned. Suboccipital decompression is rarely relieved the pressure on an obstructed aqueduct sufficiently to permit free drainage, and then for only a brief period. Passage of a catheter through the compressed aqueduct, with a length of buried rubber tubing left in place to keep the channel between the third and fourth ventricles open has occasionally been successful (Dandy, 2).¹ In view of the frequent distortion and obliteration of the aqueduct, the passage of a catheter up into the third ventricle often involves forcing a passage blindly through the surrounding structures of the mesencephalon. According to Dandy (3) the older method of puncturing the corpus callosum to drain the lateral ventricle always failed because the opening in the ventricular roof remains patent for but a short time. The same has been true of attempts to drain the lateral ventricles directly into the subarachnoid space over the convexity of the hemisphere. Even if these openings in the brain substance were to remain open, the arachnoid would become adherent at their edges so that spinal fluid could not enter the general subarachnoid space. Coagulation of the choroid plexus (Putnam), which occasionally permits the destruction of a sufficient amount of the plexus in infants with hugely dilated ventricles, is not satisfactory in adults with less extreme degrees of hydrocephalus.

¹In a subsequent article Dandy (3) stated that "strictures of the aqueduct of Sylvius recur after any attempt to restore the lumen." In Dandy's reported cases he subsequently removed the buried section of catheter. Dr. W. J. Mixer in this hospital has left the tubing in place in a single case with at least partial relief (unpublished data).

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Fig. 3. Air studies in Case 2. a, left, Encephalogram illustrates normal fourth ventricle with obstruction of the aqueduct, which is outlined by dots. b, Ventriculogram



shows enlargement of lateral and third ventricles. The upper end of the aqueduct ends in ballooning dilatation at tip of arrow (brought out by dotted line).

Figure 2, a photograph taken postmortem in Case 2 illustrates a wide open stoma 7 weeks after operation. In the 3 other adult cases in which postmortem examinations were performed the stoma was found to be patent and draining successfully in every instance. A subdural fluid collection, as reported by Dandy in his cases, was seen in a single case of infantile hydrocephalus which is not included in this report, but postmortem examination in the 4 cases here described showed that the spinal fluid was confined to the subarachnoid space and was being effectively absorbed.

Our 11 patients suffered from a variety of conditions ranging from apparently benign obstructions of the Sylvian aqueduct to tumors which arose in the region of the third ventricle, brainstem, and cerebellum (Table I). Of these patients 2 have regained useful vision and are alive and well 2½ years to 15 months after operation (Cases 1 and 9). When last heard from these patients were leading normal lives. The most dramatic result was obtained in the first case.

CASE. Mrs. L. S., aged 30 years, had noticed headaches of increasing severity for three years, and in addition rapid loss of vision over a period of 15 months. Examination on admission showed papilledema of 3 diopters. Her retinal hemorrhages, and visual acuity reduced to 20/200 in the right eye and 20/50 in the left. The neurological examination was normal. As her spinal fluid pressure was below 200, pneumoencephalogram was performed and showed clear-cut block of the Sylvian aqueduct just above the fourth ventricle (Fig. 3a). A subsequent carotidogram demonstrated marked dilatation of the lateral and third ventricles, with the aqueduct ending in ballooning dilatation 1 centimeter below the pineal body (Fig. 3b). The long history of headaches and the appearance of the block in the x-ray film strongly suggested benign occlusion

of the Sylvian aqueduct. Third ventriculostomy by the suprachiasmatic route was therefore carried out on March 1938. The following is an excerpt from the operative note:

After the usual right frontal craniotomy the dura along the floor of the anterior fossa was elevated and opened off back toward the sphenoid ridge. Tapping of the ventricle relieved the tension of the brain and thereafter it was easy to free up the entire optic chiasm and both optic nerves, as well as to expose the region just above the chiasm and the lateral carotid, middle, and anterior cerebral arteries on the right. With these landmarks all in view the bluish thinned-out shell of the third ventricle just above the chiasm was perforated. A large amount of ventricular fluid escaped. This opening, as enlarged until it was nearly 1 centimeter across. Finally puncture was made in the posterior floor of the third ventricle. It could be felt beneath the tip of the upper probe cut through the posterior wall and entered the interpeduncular cistern. This part of the operation was bloodless. After adequate hemostasis had been established the dura, bone and scalp were returned to the usual manner.

The patient made most satisfactory recovery and was discharged after 9 days. During this short period her papilledema had receded to striking degree. Within a period of 5 weeks the patient's visual acuity had recovered to 20/20 in the right eye and 20/5 in the left. When seen 10 months later visual acuity remained the same. Both optic discs are flat, but marked trophic pallor on the right. Since then, although the patient has reported no serious occurrences by letter, stating that she remains free from headaches, has retained useful vision, and is able to lead normal life. The last report as received on November 14, 1940, 1 year and 8 months after her operation.

Four other patients (Cases 4, 7, 8, and 11) were relieved of hydrocephalus. The first of these were unfortunately operated upon too late to save vision. The third died months later in another hospital of bronchopneumonia, and permission to perform a postmortem could not be obtained. The fourth was the only patient in

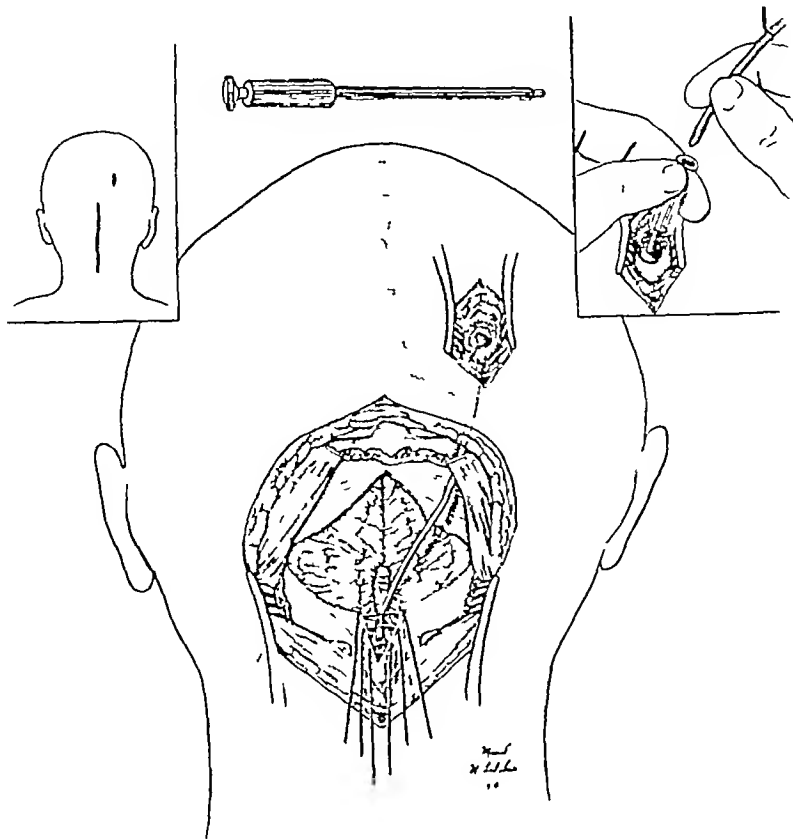


Fig 4. Technique of Torkildsen ventriculostomy. The inserts illustrate incisions for the suboccipital craniotomy and insertion of catheter in right lateral ventricle (upper left), the trocar for inserting catheter into the ventricle (upper center). Technique of inserting the catheter. Note the thread that has been tied to the catheter to serve as depth marker and to suture to the galea after the trocar

has been withdrawn (upper right). In the main drawing the stitches are shown which are used for anchoring the lower end of the catheter into the cisterna magna and closing the dura. The arachnoid covering the cisterna has not been sketched, but it is important to include this membrane in the sutures in addition, as the description in the text indicates.

failed to show a reduction in intracranial pressure to a normal level. This was due to a large cavernous hemangioma of her left temporoparietal lobe with extension to the basal ganglia. This tumor not only compressed the aqueduct, but raised the intracranial pressure by its great size. A subsequent partial removal of the mass resulted in the patient's death.

Three patients died as a result of operation, making a case mortality of 27 per cent. These included Case 3 in which patient died of pulmonary embolism, and Cases 5 and 6, in which patients developed complicating postoperative hematomas. Death in Cases 2 and 10 was due to compression of vital centers by the tumor, which continued after the obstructing hydrocephalus had been relieved.

Before Torkildsen reported his ingenious operation we drained the obstructed ventricular system

through the anterior route in cases in which a previous posterior exploration or strong clinical and ventriculographic evidence pointed to an inoperable lesion as the cause of the obstruction. But the bitter experience of missing a cystic hemangioblastoma of the cerebellum in Case 2, in which air injection had indicated a tumor of the midbrain, taught us the risk of relying on ventriculographic evidence for the exclusion of an operable lesion in the posterior fossa.

CASE 2. H S., a 6 year old girl, entered the Children's Service after 10 months of headache and vomiting. She had a bilateral sixth nerve paresis, with spastic weakness of her left leg and arm, as well as of the right leg. At first there was only slight papilledema and no nystagmus or signs of cerebellar pathology. Her pupils reacted very sluggishly both to light and accommodation. Flat skull plates showed increased convolitional markings and widened cranial sutures. On the supposition that these symptoms and signs were due to occlusion of the fourth ventricle by a medulloblastoma, a trial of radiation therapy was in



Fig. 5. Postoperative ventriculogram. Its catheter in position.

silk suture and continued for several weeks, but without any improvement.

The girl, as first seen in consultation by one of us (J. C. W.) at the end of this period. She was then semi-stuporous and in too poor condition for satisfactory neurological examination. One additional observation of interest, which had not been recorded previously, was that upward movement of her eyes appeared to be limited. A ventriculogram was performed and suggested obstruction of the aqueduct near its upper end, "probably due to tumor which lies mainly to the floor of the aqueduct. As believed that tumor in this situation is inoperable, anterior drainage of the third ventricle was performed through suprachiasmatic approach on August 2, 1935.

Following operation the patient made a surprisingly good recovery and regained the use of her extremities. The signs of increased intracranial pressure disappeared. When the left ventricle was tapped only 40 cubic centimeters of xanthochromic fluid escaped at normal pressure, whereas before operation the pressure had been over 400 millimeters B. P. In spite of the relief of the obstructive hydrocephalus she began to develop signs of cerebellar pathology a month later. Its evidence of compression of the vital medullary centers, which caused her death 14 months later.

Postmortem examination revealed satisfactory relief of hydrocephalus, with wide open stoma through the basilar tentorium above the optic chiasm (Fig. 6). Comparison of the preoperative ventriculogram with postoperative measurements of the ventricles showed striking reduction in their size. The cause of death was bilateral bronchopneumonia, secondary to compression of the brain stem by cystic hemangioendothelioma of the left cerebellar hemisphere. The primary lesion could have been easily attacked and the compression of the aqueduct relieved if suboccipital exploration had been made soon after her admission.

As a result of this unfortunate experience we have reached the conclusion that ventriculostomy through the anterior wall of the third ventricle should not be performed unless both clinical and laboratory evidence point unquestionably to the

presence of an obstructing lesion which is inoperable because of its situation, or unless this diagnosis has been established at a previous exploration. Under these circumstances, as in Cases 1, 3, 4, 5, 6, 10 and 11 this form of ventriculostomy could seem to be the most satisfactory operation. Had we known of Torkildsen's approach sooner we should have preferred this in Cases 2, 7 and 9, in which the cause of obstruction was uncertain. This valuable procedure, as will be seen, permits the surgeon to explore the posterior fossa as a preliminary to permanent ventricular drainage. In Case 8 with otitic hydrocephalus an occipital operation could not have been considered in any case because of the presence of a septic mastoid wound.

DRAINAGE OF LATERAL VENTRICLE INTO THE CISTERNA MAGNA—TORKILDSEN OPERATION

A standard suboccipital craniectomy is performed through a midline longitudinal incision in the scalp and upper neck. If the cervical fascia is cross cut just below its insertion in the occipital bone there is no need to make a cross-bow incision in the scalp. After scraping the muscles off the bone low enough to expose the arch of the atlas vertebra, this portion of the occiput and the arch of the atlas are ringed away. The dura is next opened crucially. In opening the arachnoid over the cisterna magna it is important to incise it longitudinally and then to use every precaution to preserve the two lateral flaps of arachnoid and dura intact, so that the cistern can be reconstructed in the subsequent closure. The surgeon is then in a position to make a thorough exploration of the posterior fossa and also to test the patency of the aqueduct by determining whether it will admit the passage of a fine soft rubber catheter. In the face of an inoperable high tumor or an occlusion of the aqueduct Torkildsen recommended the following procedure. If an occipital burr hole for decompression of the ventricular system has not been made as preliminary to opening the tense cerebellar dura, a small trephine opening is made in the occipital bone 3 centimeters above the tentorium and directly over the posterior horn of the right lateral ventricle. The position of the posterior horn is first ascertained by puncture. As the ventricular needle is withdrawn, trocar 4 millimeters in diameter is inserted along its tract. When the stylet is pulled out the metal sleeve serves as a guide for insertion of a No. 8 soft rubber catheter. Before this is slipped into the ventricle an extra eye should be cut close to its tip and a silk suture tied around it to serve as a depth marker and for later suture

Following the metastatic diagnosis in this patient, no further patients have been subjected to exploratory trial of radiation for medulloblastoma without previous verification by exploration and biopsy.

of the catheter to the galea at its point of exit from the skull. The catheter tip should be thrust 2 to 3 centimeters into the ventricular cavity. The metal sleeve is then removed and the rubber tube sutured firmly to the galea. When this maneuver has been completed, a tunnel is made between the galea and cranium to permit the passage of the catheter from the small separate incision over the trephine opening to the larger midoccipital one. This can be carried out without difficulty by separating the tissues with a large curved hemostat, seizing the lower end of the catheter, and drawing it back through the resultant tunnel. The catheter is now cut off so that its lower end just reaches the cisterna magna (Fig 4). This is then reconstructed as accurately as possible over the tube by suturing together the two lateral flaps which were saved for this purpose. Burying and securely fixing the end of the catheter beneath the arachnoid is perhaps the most important part of the operation. It can be accomplished best if the surgeon plans his incision carefully as he opens the dura and arachnoid overlying the cistern. In reconstructing these membranes we have passed fine silk stitches through the dura, arachnoid, and outer layer of catheter, and then out through the same layers in reverse order. Both incisions are then closed in layers with silk sutures. When the dressing is applied a checkrein of adhesive tape is incorporated in it from vertex to shoulder blades to prevent forward flexion of the head for the first few days. Figure 5 illustrates the position of the catheter in the first patient, with the ventricles outlined by air injection 12 days after operation.

The three adult patients who have been submitted to this operation in the advanced stage of hydrocephalus with intense headache, vomiting, high grade papilledema, and increasing somnolence have recovered and remained relieved of their obstructive symptoms for periods ranging from 5 to 18 months. The striking improvement which may follow the institution of permanent drainage by a buried catheter is summarized in Table II and in the history of the following patient.

CASE 13 T. K., a 21 year old man, entered the hospital with a 10 months' history of headache, chiefly in the occipital region. Three weeks before admission his headaches had become increasingly severe and incapacitating. For several days before entry he held his head rigid because of the pain, but he was able to walk without apparent unsteadiness. He complained of episodes of nausea but had not vomited. Recently his family had noticed increasing irritability and slowing of his speech, but no definite change in his mentality.

On examination the patient was sluggish mentally and held his neck in slight extension. His breathing was slow and labored. Ophthalmoscopic examination revealed 4 to 5

diopters of choking, with small striate hemorrhages above both discs and a small hemorrhage in the right macula. His vision was very poor, particularly in the right eye, and the rough field determinations were normal, but his condition was too critical to permit accurate examination. There were no outstanding cerebellar signs and no nystagmus, but a suggestive impairment in upward deviation of the eyes. Otherwise the cranial nerves were normal. This was also true of the spinal reflexes as well as of the motor and sensory examinations.

Because of threatened respiratory paralysis, occipital burr holes were made on the evening of his admission. The next morning a cerebellar exploration was performed with Torikildsen drainage of his right lateral ventricle into the cisterna magna. The operative note reads as follows:

"Under general anesthesia a ventricular needle was inserted through the right sided burr hole made last night. The ventricle was easily entered and proved to be large, containing over 75 cubic centimeters of fluid under high pressure (200+). This having been ascertained, the safest course appeared to be a cerebellar exploration and palliative drainage of the hydrocephalus, if no operable tumor were found. The patient was therefore placed in cerebellar position, and through a midline incision the occipital muscles were cross-cut and a broad area of occiput was exposed. This was removed together with the arch of the atlas. After the dura had been opened, the cerebellar hemispheres were seen to be symmetrical and the vermis not widened. Only a small pressure cone was present. The cerebellum was not tense because the needle had been left in the lateral ventricle. After separation of the cerebellar tonsils one could look upward into a normal appearing fourth ventricle. A No. 10 catheter slipped up the aqueduct met a definite obstruction at a point 4 to 5 centimeters above the lower end of the fourth ventricle. When the anesthetist gave jugular compression, no fluid escaped from above, suggesting that the site of obstruction lay in the upper portion of the aqueduct in the region of the quadrigeminal plate, and that it would be inaccessible to surgery from below. Therefore the palliative procedure described by Torikildsen was carried out. The tip of a No. 8 catheter was buried in the posterior horn of the ventricle and the tube was then passed underneath the scalp from the incision over the burr hole to the median cerebellar incision. Its other end was carefully sutured beneath the arachnoid and dura in the cisterna magna. We were very careful to ascertain that spinal fluid flowed freely out of the tube before closing the arachnoid and dura. The neck muscles were then carefully resutured to the occiput and to each other in the midline. This procedure was tolerated well, blood pressure remaining at a normal level throughout."

The patient was in good condition after operation, and on the fourth day his lumbar and intraventricular pressure readings were normal. Phenolsulfonphthalein was injected into the ventricle and 10 per cent recovered in the urine in the next 2 hours. A ventriculogram carried out 3 weeks later showed free drainage from the previously obstructed ventricles, as all the gas was found distributed over the subarachnoid space. Five days afterward a second ventriculogram was undertaken, 1 cubic centimeter of phenolsulfonphthalein was injected first, followed by 90 cubic centimeters of oxygen. The injection displaced spinal fluid from the ventricles and this was drained through a second needle in the lumbar subarachnoid space. The rapid appearance of dye in the fluid recovered in the lumbar region and a previous pressure reading of 105 millimeters established the patency of the artificial drainage system. The subsequent x-ray films showed a symmetrical dilatation of the lateral and third ventricles without any visible filling of the aqueduct. Beginning on the twenty-fifth postoperative

TABLE 1 RESULTS OF THIRD VENTRICULOSTOMY THROUGH THE LAMINA TERMINALIS IN THE TREATMENT OF OBSTRUCTIVE HYDROCEPHALUS

Case	Symptoms	Neurological examination	Optic discs	Vision	Oversees (visual evoked potentials)	X-ray	Discharge	Operation	End result
No. 1 Lambert 1947 Age 30	Unilateral attacks of vomiting and drowsiness of weeks, 1939	Unilateral optic atrophy	Peripapilledema	O.D. 1 only M.D. 1 only perimetry	+	Obstruction of aqueduct with normal hydrocephalus	Obstruction of aqueduct	3rd ventriculostomy	Lamella normal size for 15 years. Resolved vision 10/20, 10/20
No. 2 Holt 1948 Age 40	Headache and vomiting 9-10 times	Bilateral optic atrophy	Peripapilledema	Completely normal	+	Obstruction of aqueduct	Hydrocephalus	3rd ventriculostomy	Relief of hydrocephalus and end of vomiting 6 yrs.
No. 3 Vaccaro 1949 Age 40	Headache and vomiting 10 times. Attacks of unconsciousness with focal extension of electrical activity, and epileptiform discharges.	Dilatation, cloudy with serum, bilateral optic atrophy, and focal epileptiform discharges	Bilateral blurring	Impairment to test	+	Partial atrophy of optic nerves and normal ventricles	Peripapilledema	3rd ventriculostomy	Relief from headache and vomiting. Head normal. No further attacks of unconsciousness. No epileptiform discharges. Normal intelligence of normal vision and personality unchanged
No. 4 Thompson 1949 Age 40	Altered mental state, loss of consciousness, and focal epileptiform discharges	Unilateral optic atrophy and normal vision	Peripapilledema	Very poor	+	Dilatation of lateral ventricles and 3rd ventricle. Normal ventricles and normal ventricles	Obstruction of aqueduct	3rd ventriculostomy	Relief from headache, unconsciousness, and focal epileptiform discharges. Vision 10/20, 10/20
No. 5 Chapman 1949 Age 40	Headache and vomiting 10 times. Unconsciousness and focal epileptiform discharges	Wide based optic atrophy, and normal vision	Peripapilledema	10/20, 10/20	+	Increased blood vessel in optic nerve. Unilateral optic atrophy and normal ventricles	Obstruction of aqueduct	3rd ventriculostomy	Relief from headache and vomiting. Vision 10/20, 10/20
No. 6 Vaccaro 1949 Age 40	Headache and vomiting 10 times. Unconsciousness and focal epileptiform discharges	Unilateral optic atrophy, and normal vision	Peripapilledema	10/20, 10/20	+	Unilateral hydrocephalus and normal ventricles	Obstruction of aqueduct	3rd ventriculostomy	Complete relief from headache and vomiting. Vision 10/20, 10/20
No. 7 Baker 1949 Age 40	Headache and vomiting 10 times. Unconsciousness and focal epileptiform discharges	Unilateral optic atrophy, and normal vision	Peripapilledema	10/20, 10/20	+	Unilateral hydrocephalus and normal ventricles	Obstruction of aqueduct	3rd ventriculostomy	Complete relief from headache and vomiting. Vision 10/20, 10/20
No. 8 Chapman 1949 Age 40	Headache and vomiting 10 times. Unconsciousness and focal epileptiform discharges	Unilateral optic atrophy, and normal vision	Peripapilledema	10/20, 10/20	+	Unilateral hydrocephalus and normal ventricles	Obstruction of aqueduct	3rd ventriculostomy	Complete relief from headache and vomiting. Vision 10/20, 10/20

TABLE I RESULTS OF THIRD VENTRICULOSTOMY THROUGH THE LAMINA TERMINALIS IN THE TREATMENT OF OBSTRUCTIVE HYDROCEPHALUS—Continued

Case	Symptoms	Neurological examination	Optic discs	Vision	Cerebrospinal fluid pressure	X ray	Diagnosis	Operation	End result
No 9 Agnes S 1889/68 Age 44	Intermittent headache vomiting visual disturbances ataxia 6 yrs	Drowsy pupils fixed L and A distur- bance of upward gaze, L facial weakness R Babinski	Papilledema, L > R.	20/20	20/70	270	Dilatation lateral and 3rd ventricles no air in aqueduct or 4th ventricle	3rd ventriculostomy	Feeling well and doing housework 15 mos after operation. Local neurological signs slowly progressing. No papilledema. Cerebrospinal fluid pressure low
No 10 Alma De M 207008 Age 16	Headache, generalized convulsions unstead- iness weight increase, bilateral flaccid choreiform movements	Obesity with strab- ismus limited upward gaze, no reaction to light, poor converg- ence slight R. facial weakness falling backward and to left when walking	Papilledema, 2 3 D	20/50	20/40	—	Calcified tumor in region of the pial margin	3rd ventriculostomy	Improved but died suddenly during a course of x ray treatment
No 11 Mary S 108339 Age 16	Headache and dizziness 3 weeks Fall with confusion exacerba- tion of headache and pain between eyes 4 days	Weakness of L. III & VII nerves rigidity of neck, spasticity of legs ? R. Babinski Other reflexes nonco-ordinatory	Slight papil- ledema	20/200	20/200	400	Dilatation of both lateral ventricles and of 3rd ventricle, with mass protruding into L. lateral ventricle and compressing aqueduct	1 3rd ventriculostomy 2 Intraventricular exploration	Died 17 days after second operation from bronchopneumonia

TABLE II RESULTS OF TORKILDSEN OPERATION IN THE TREATMENT OF OBSTRUCTIVE HYDROCEPHALUS

Case	Symptoms	Neurological examination	Optic discs	Vision	Cerebrospinal fluid pressure	X ray	Diagnosis	Operation	End result
No 12 Evelyn M 215812 Age 32	Vomiting, intermittent occipital headache, black spots in R. eye numbness and weak- ness R. leg and hand	Disturbance of con- jugate eye move- ments nystagmus buzzing to both ears hyperaesthesia to pin prick R. side	Papilledema, 3 D	O D 20/30	O S 20/200	Not obtained	Postoperative ventri- culogram shows obstruction high in aqueduct	Exploration of posterior fossa with catheter drainage (Torkildsen)	Gradual disappearance of symptoms except for nystagmus and occasional headaches Several series of x-ray treatments. Returned to work and leading normal life at 18 mos
No 13 Thomas K 220726 Age 21	Occipital headaches nausea, rigidity of neck, disturbance of vision irritability, and slowing of speech, 8 mos	? Impairment upward gaze Mentally sluggish Head in slight extension. Breathing slow and labored	Bilateral papille- dema 4 5 D with hemor- rhages	Not tested	Not obtained	Flat plates not con- tributory, no pre- operative air injection	Obstruction of aqueduct, ? tumor	Exploration of posterior fossa with catheter drainage (Torkildsen)	Gradual disappearance of all symptoms Returned to work at 11 mos
No 14 Paul Z 09361 Age 51	Headache and increas- ing difficulty with walking	Not co-operative very drowsy, limita- tion of upward and lateral gaze, some disturbance of co-ordination	Papilledema	20/40	20/30	1) 85 2) 200 3) 215 Xantho- chromic 90 rbc.	? Obstruction of aqueduct	Exploration of posterior fossa with catheter drainage (Torkildsen)	Lives a fairly normal life at home at 4 mos

TABLE I RESULTS OF THIRD VENTRICULOSTOMY THROUGH THE LAMINA TERMINALIS IN THE TREATMENT OF OBSTRUCTIVE HYDROCEPHALUS—Continued

Case	Symptoms	Neurological examination	Optic discs	Vision	Cerebro-spinal fluid pressure	X ray	Diagnosis	Operation	End result
No. 6 Ames S 185008 Age 44	Intermittent headache vomiting, visual disturbances ataxia 6 yrs	Drowsy pupils fixed L and A, disturbance of upward gaze, L facial weakness R Babinski	Papilledema, L > R	20/20 20/70	270	Dilatation lateral and 3rd ventricle, no air in aqueduct or 4th ventricle	Midbrain tumor	3rd ventriculostomy	Feeling well and doing housework 15 mos after operation. Local neurological signs slowly progressing No papilledema Cerebrospinal fluid pressure low
No 10 Alma D M 209008 Age 16	Headache, generalized convulsions unstead- iness weight increase, bilateral tinnitus, choreiform movements	Obesity with strab- ismus limited upward gaze, no reaction to light, poor conver- gence, slight R facial weakness falling backward and leg left when walking	Papilledema, 2 3 D	20/30 20/40	—	Calcified tumor in region of the pineal	Pinealoma (postmortem)	3rd ventriculostomy	Improved but died suddenly during a course of x ray treatment
No 17 Mory S 108009 Age 16	Headache and dizziness 3 weeks Fall with confusion exacerba- tion of headache, and pain between eyes 4 days	Weakness of L III & XII nerves rigidity of neck, spasticity of legs ? R Babinski Other reflexes noncontributory	Slight papil- ledema	20/200 20/200	400	Dilatation of both lateral ventricles and of 3rd ventricle, with mass protruding into L lateral ventricle and compressing a aqueduct	Cavernous hemangioma of choroid plexus	1 3rd ventriculostomy 2 Intra-ventricular exploration	Died 17 days after second operation from bronchopneumonia

TABLE II RESULTS OF TORKILDSEN OPERATION IN THE TREATMENT OF OBSTRUCTIVE HYDROCEPHALUS

Case	Symptoms	Neurological examination	Optic discs	Vision	Cerebro-spinal fluid pressure	X ray	Diagnosis	Operation	End result
No. 12 Evelyn M 215812 Age 32	1 vomiting, intermittent occipital headache black spots in R eye numbness and weak- ness R leg and hand	Disturbance of con- jugate eye move- ments nystagmus buzzing in both ears hyperesthesia to pin- prick R side	Papilledema 3 D	O D 20/30	Not obtained	Postoperative ventri- culogram shows obstruction high in aqueduct	Obstruction of aqueduct, ? tumor of brain stem	Exploration of posterior fossa with catheter drainage (Torkildsen)	Gradual disappearance of symptoms except for nystagmus and occasional headaches Several series of x ray treatments. Returned to work and leading normal life at 18 mos
No 13 Thomas A 220726 Age 21	Occipital headaches, nausea, rigidity of neck, diminution of vision irritability and slowing of speech 8 mos	? Impairment upward gaze Mentally sluggish Head in slight extension. Breathing slow and labored	Bilateral papil- ledema 4 5 D with hemor- rhages	Not tested	Not obtained	Flat plates not con- tributory no pre- operative air injection	Obstruction of aqueduct, ? tumor	Exploration of posterior fossa with catheter drainage (Torkildsen)	Gradual disappearance of all symptoms Returned to work at 11 mos
No 14 Paul Z 09301 Age 51	Headache and increas- ing difficulty with walking	Not co-operative very drowsy, limita- tion of upward and lateral gaze some disturbance of co-ordination	Papilledema	20/40 20/30	1 85 2 190 3 215 Xantho- chromic 90 rbc	? Obstruction of aqueduct	Obstruction of aqueduct, ? midbrain tumor	Exploration of posterior fossa with catheter drainage	Lives a fairly normal life at home at 4 mos

day x-ray therapy was given in six equal doses. At the time of discharge the last traces of papilledema were disappearing, and vision had recovered to 20/20 and 20/20. There was still impairment of upward gaze, suggestive of mid-brain lesion.

Since discharge the patient has made most satisfactory recovery. At his last follow-up examination on September 25, 1940 (months after operation) he appeared to be in excellent health. He complained of no headaches or other symptoms of intracranial pathology. If he stood up suddenly there was momentary unsteadiness, but otherwise his gait and movements were normal. He had recovered full upward movement of the eyes and showed no neurological abnormality. Except for slight pallor of the right optic disc, ophthalmoscopic examination showed normal conditions. The patient left that his vision had fully recovered. He planned to return to his previous occupation as a clerk.

SELECTION OF OPERATION

Both methods of draining the obstructed ventricles here reported appear to accomplish their purpose in an effective and lasting manner. The obstructed cerebrospinal fluid is drained into the large arachnoid cisterns, whence it can be distributed to the absorbing areas in the subarachnoid space in a normal fashion. It is obvious that these procedures can be effective only in the obstructive form of hydrocephalus. In the communicating type, in which basilar cisterns or absorbing areas in the cranial subarachnoid space are obliterated, nothing can be accomplished by these operations. This variety of hydrocephalus can be diagnosed by the history of a recent meningococcal infection. It can be verified by the fact that phenolsulfonphthalein injected into the ventricles appears in the lumbar region, although very little is absorbed in the blood stream and eliminated by the kidneys (Dandy and Blackfan, 6).

In choosing the most suitable method of ventricular drainage it is of great importance to localize the obstructing lesion as accurately as possible. In most cases this can be done by clinical and x-ray examination. In Case 2 a block in the sylvian aqueduct was clearly visible after the combined injection of oxygen into the lateral ventricles and lumbar subarachnoid space (Fig. 3). Pneumoencephalography however is often too dangerous to use in patients with elevated intracranial pressure. Ventriculography alone usually gives accurate localization in the presence of a tumor in the third ventricle, but may be misleading in infratentorial lesions. This led to an unfortunate result in the second patient, in whom an upward projection of the mesencephalon was mistaken for a midbrain tumor whereas actually the deformity was caused by an operable cystic tumor of the cerebellum. We recommend drainage of the third ventricle only if previous exploration or

the combined evidence of clinical and radiological examination has demonstrated beyond a doubt that the obstructive lesion cannot be attacked directly.

The method of Torikildsen has the strategic advantage of permitting preliminary exploration of the posterior fossa before the institution of palliative drainage of the obstructed cerebrospinal fluid. It is surprising that the presence of a rubber catheter embedded in the cisterna magna is not followed by rapid closure of its open end by arachnoid adhesions. Fortunately this has not proved to be the case as shown by Torikildsen's experience and the long-standing relief in the 3 cases here reported. Although unlikely it is still possible for occlusion to occur or for the rubber to deteriorate after a number of years. Should either of these complications take place, drainage can again be re-established through the supratentorial route. This operation does not involve the insertion of a foreign body and appears to be a more physiological procedure in cases in which, in the posterior portion of the third ventricle or below there is an obstruction which cannot be corrected surgically.

SUMMARY AND CONCLUSIONS

1. Two effective operations have been reported in recent years for the drainage of the ventricular system in cases of obstructive hydrocephalus in adults.

2. The first method consists of perforating the thin, bulging anterior wall of the third ventricle (lamina terminalis) and establishing drainage of the obstructed cerebrospinal fluid into the chiasmatic cistern. In certain cases it is also possible to perforate the floor of the dilated third ventricle posteriorly thereby creating a second drainage channel into the interpeduncular cistern. From our experience we believe that this additional opening is not essential and should not be attempted unless it can be carried out with ease and safety.

3. In the second method which is carried out only after exploration of the posterior fossa has revealed an inoperable lesion, the cerebrospinal fluid is short-circuited past the obstruction in the aqueduct, third or fourth ventricle by means of a buried rubber catheter. The tip of the catheter is inserted through an occipital trephine opening and fixed in the posterior horn of the lateral ventricle. The rubber tube is then passed beneath the scalp to the cerebellar incision and its lower end is buried in the cisterna magna.

4. As the latter operation permits a preliminary exploration of the posterior fossa, it is the more

effective method of dealing with cases of hydrocephalus in which the cause of obstruction may be an operable tumor situated in the cerebellum or fourth ventricle, or an arachnoiditis which blocks the outflow of cerebrospinal fluid. On the other hand, when the obstruction is known to be inoperable and is situated in the posterior portion of the third ventricle or caudal to this point, anterior drainage through the lamina terminalis is the more satisfactory operation.

5 Both methods are capable of producing a long lasting channel for escape of the obstructed cerebrospinal fluid into the subarachnoid space, with relief from the symptoms of elevated intracranial pressure and its dangers to life and vision. This is exemplified by the case histories of 14 patients whom we have treated in this way. The hydrocephalus has been relieved in all. Life has been preserved in 7 and useful vision has been established in 5, 4 have been able to return to work and remain in good condition after intervals of 18 months to 3 years.

ADDENDUM

Since this manuscript was sent in for publication we have received reports from Dr F D Ingraham and Dr W J German of 3 other patients with obstructive hydrocephalus on whom the Torkildsen operation was performed. These cases are so instructive that brief résumés of their histories have been added. We wish to thank these surgeons for their kindness in permitting us to include this interesting material.

1 A girl of 5 entered the Children's Hospital with a story of high intracranial pressure and cerebellar signs. In the course of study it was shown that she had a block at the upper end of the aqueduct. Dr Ingraham reports that he "explored this region by dividing the tentorium and exposed a medulloblastoma. A small piece of tissue only was removed for section, and when the diagnosis was verified she was given a course of radiation. The division of the tentorium and the effects of the radiation were not sufficient to relieve the block, and a Torkildsen procedure was carried out. This patient died 14 months after this last operation. There is no question but that the bypass restored her to comparatively good health and gave her a much more satisfactory survival period than she would have had otherwise. We have now had an opportunity to study the brain and the local examination was extremely interesting. The tube was quite unchanged in appearance. It was patent and there was a reservoir at the lower end into which fluid was obviously passing from the ventricle. Death was presumably due to local increase in size of the tumor which made it impossible for fluid to pass from the cisterna magna into the subarachnoid area over the cortex."

2 Dr Ingraham's second patient was a boy 6 years of age with a typical midline cerebellar syndrome and obstructive hydrocephalus. "At operation he was found to have a

block in the aqueduct, although no tumor was exposed, and it was taken to be a congenital abnormality. The Torkildsen procedure was carried out and he was watched for 3 months. His pressure remained normal during that time, and after a short trial of clamping the tube through a small incision we thought that he might have stabilized and removed the tube. In a very short time his pressure was elevated again and the tube was replaced. For several months he had a rather large collection of fluid in the region of his suboccipital decompression. This has returned to normal contour and his pressure has stayed within normal limits. The total period of observation in this patient is also 14 months. He is now symptom free, goes to school, and takes part in ordinary activities."

3 Dr German has written us about a patient in the New Haven Hospital on whom he performed a Torkildsen operation for stenosis of the sylvian aqueduct. This girl did not maintain lasting relief of her internal hydrocephalus so that 5 weeks later it became necessary to re-explore her posterior fossa. The lower end of the catheter opened into a large smooth walled cavity in the occipital region which was completely walled off from the cisterna magna. After further exploration of the upper end of the fourth ventricle Dr German discovered a stenotic band at the lower end of the aqueduct, which he was able to cut and thereby released the obstruction.

This is the only case to our knowledge followed by secondary closure of the catheter. As we have pointed out in the article, such a complication can be corrected if necessary by a subsequent third ventriculostomy. It is better to run the risk of an occasional late closure of the tube than to lose the opportunity for a direct attack on an operable lesion through failure to explore the posterior fossa, as is the case when third ventriculostomy is done as a primary procedure.

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FINE ALLOY STEEL WIRE SUTURES

An Experimental and Clinical Study

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OF the many factors influencing the healing of surgical wounds, the reaction accompanying the use of different suture materials has been studied most extensively. The ideal suture, however is yet to be found, although catgut and silk have been employed most frequently. The superiority of the latter over the former in most circumstances has been adequately demonstrated by many experimental and clinical observations (6, 7, 9, 10, 11, 13, 14, 15). However, in the presence of infection, the silk suture may act as a nidus for the organisms and prolong the period of healing. For this reason, many surgeons still prefer catgut and even the most ardent advocates of silk (6, 7, 14) warn against its use in infected wounds. In 1934, Babcock (1) proposed the use of fine alloy steel wire as a permanent suture material. Because of its fine caliber, smooth surface, nonpermeability and chemically stable nature, he claimed that this material was satisfactory for use in both aseptic and infected wounds. This author's subsequent experience seemed to substantiate these claims (2, 3, 4). Also, Kaufman, Johnson, and Lesser in an analysis of 56 cases of hernioplasty found the incidence of wound infection to be much lower in the group of cases in which wire sutures were employed than in the groups closed with catgut or silk. Bunnell reported favorable results from the use of wire sutures in the repair of tendons. Preston demonstrated experimentally in rats that wounds sutured with fine wire had a greater tensile strength than that of similar wounds sutured with catgut or silk. In view of these encouraging reports we were led to investigate further the behavior of fine alloy steel wire when employed as a suture material in both animal and human tissues and to attempt to estimate its relative merits in comparison with the more commonly used materials.

EXPERIMENTAL STUDY

Four groups of experiments were conducted in order to compare the tissue reaction produced by alloy steel wire sutures with that produced by

silk or catgut sutures in both aseptic and infected wounds. The wire employed in all of the experiments was size 35. It is a whitish pliable hair-like string having a diameter of 0.0007 of an inch and a tensile strength of 25 pounds (1).

Group 1: Tissue Reaction in Aseptic Wounds

Procedure. Incisions 5 centimeters in length were made in the abdominal wall of dogs deeply enough to expose the anterior sheath of the rectus muscle. Three interrupted sutures of the alloy steel wire were applied through the rectus sheath and a part of the muscle in each wound. Three similar sutures of either silk or catgut were applied in the same wound for the purpose of comparison and control. All of the sutures were applied with fine curved needles of the same size. The wounds were reopened at different intervals after the operation and gross changes around the sutures were noted. This was followed by the excision of blocks of fascia and muscle bearing the sutures, for the purpose of microscopical study. The specimens were fixed in a 10 per cent solution of formalin. The wire sutures were removed after the fixation and sections were made through the fascia and the muscle at the places through which the sutures had passed. All sections were stained with hematoxylin and eosin. The control sutures consisted of silk, both No. C (medium silk) and No. A (fine silk) grades; plain catgut, No. 1 and No. 00 and chromic catgut, No. 1 and No. 00. Observations were made at periods varying from 24 hours to 20 days after original application of sutures. Altogether 21 wounds were studied.

Gross examination. *Wire sutures.* In recent wounds, no inflammatory reaction was observed in the tissues around the sutures. However, most of the sutures appeared tighter than at the time of the original application, causing a slight constriction of the fascia. In the wounds more than 1 week old, the wire was covered by a thin layer of fibrous tissue. Staining or necrosis of tissues around sutures was not noticed and the color and luster of the wire remained practically unchanged.

Silk sutures. Slight to moderate edema and necrosis were observed in wounds 2 and 5 days

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old Although of less intensity than those observed around the catgut sutures, these changes, in contrast to those around the wires, were very distinct. After 9 days, the sutures were found to be buried in a rather heavy layer of fibrous tissue. In a few specimens, a small amount of cloudy fluid was found around the sutures as long as 20 days after they had been applied.

Catgut sutures Moderate edema, slight necrosis, and a small amount of turbid exudate were invariably observed around the catgut sutures in wounds less than 5 days old. The reaction around the plain catgut was especially marked. That around the No. 00 sutures was slightly less than that around the No. 1 sutures of both plain and chromic gut. Plain catgut began to show evidence of disintegration on the fourth or fifth day and usually had totally disappeared after 7 days. The chromic catgut sutures were fairly well preserved for the first 2 weeks, after 20 days they were found to have disappeared.

Microscopic examination. Wire sutures Sections of tissue from 24 hour to 3 day old wounds showed the presence around each suture of a thin layer of hyalinized material probably formed as a result of compression of the tissues by the sutures. In the surrounding tissue, there was slight leucocytic infiltration, some edema, and occasionally a small amount of fibrinous exudate. In the 4 day wound there was slight proliferation of fibroblasts and infiltration with lymphocytes and plasma cells in the neighborhood of the sutures. In the wounds more than 7 days old, the number of fibroblasts decreased while the amount of intercellular collagen fibrils increased. Granulation tissue was not observed. Aside from some atrophy of the muscle fibers in immediate neighborhood, there was no other evidence of damage to tissues.

Silk sutures The tissue reaction to the No. A silk was less than that to the No. C silk sutures. However, the difference was not marked, and they are described together. In wounds less than 5 days old the sutures were surrounded by some necrotic tissue infiltrated by a large number of leucocytes. In the non-necrotic tissue in the neighborhood there was moderate leucocytic, and occasionally also fibrinous, exudate. After 5 days the acute inflammatory reaction began to subside. However, among the filaments of the sutures there usually were some leucocytes. At the same time there was fibroblastic proliferation and infiltration of lymphocytes, plasma cells, and large mononuclear phagocytes. The latter often were crowded together in close apposition to the sutures, later foreign body giant cells frequently were seen. In tissues from wounds 13 to 20 days

old, the acute inflammatory reaction usually had largely disappeared, but a few leucocytes remained among filaments of the sutures or in their immediate neighborhood. The sutures were surrounded by a broad zone of newly formed fibrous tissue.

Catgut sutures The plain and the chromic sutures of the same size caused a very similar reaction, but the finer sutures (No. 00) produced relatively less reaction than the heavier ones (No. 1). A description of the microscopic findings of the tissues sutured by No. 1 chromic catgut will suffice. A very intense and extensive acute inflammatory reaction was observed around the sutures in wounds from 1 to 5 days old. The reaction was not limited to the immediate neighborhood of the sutures but involved the adjacent tissues for some distance. There was heavy leucocytic infiltration, marked fibrinous exudation, congestion, and edema. The leucocytic infiltration was so intense around the sutures that small abscesses were often formed. The tissues surrounding the sutures, including the muscles, usually showed necrosis. In the 4 day specimens, granulation tissue began to appear and reached the maximum amount on the seventh to the ninth day. The sutures at this time still were surrounded by a zone of leucocytic exudate. The granulation tissue was infiltrated by many leucocytes, lymphocytes, plasma cells, and numerous large phagocytes containing many nuclear fragments and fatty droplets. There was no tendency for these phagocytes to form foreign body giant cells. In the specimens from wounds more than 9 to 13 days old, there was considerable fibrosis in the granulation tissue, but marked leucocytic infiltration still was observed in the immediate neighborhood of the partially absorbed catgut sutures. The majority of the sutures began to show fragmentation and penetration by leucocytes as early as the fourth or fifth day. A few appeared to be intact up to the thirteenth day.

Summary Table I summarizes the tissue reaction around the different kinds of sutures as observed at varying intervals after they had been placed in position. It will be seen that the wire sutures caused very slight initial acute inflammatory reaction followed by a slight amount of fibrosis without the formation of actual granulation tissue. The silk sutures produced a more acute inflammatory reaction, some granulation tissue and much fibrosis. The catgut sutures caused a very severe acute inflammatory reaction in the early wounds with frequent formation of minute abscesses. This was followed by extensive granulation and fibrosis. These changes are illustrated in Figures 1 to 4.

TABLE I.—TISSUE REACTIONS TO FINE ALLOY STEEL WIRE, SILK, AND CATGUT SUTURES IN ASEPTIC WOUNDS OF DOGS

Reaction	Acute inflammatory reaction								Granulation tissue								Fibrosis							
	Wire		Silk		Plain catgut		Chromic catgut		Wire		Silk		Plain catgut		Chromic catgut		Wire		Silk		Plain catgut		Chromic catgut	
Suture	K	C	K	C	K	C	K	C	K	C	K	C	K	C	K	C	K	C	K	C	K	C	K	C
Duration of wound—days	1	2	1	2	1	2	1	2	1	2	1	2	1	2	1	2	1	2	1	2	1	2	1	2
1	+				+++	++	+	++	—				—		—		—		—		—		—	
2	+	+++				++	++		—	—	—				—		—	—	—	—				
3	+				++	++			—				—						—					
4	+				++	++			—				+											—
5	+	+			++	++			—	+++	++		—		++		+		+	—				
7	—				++	++		+++	—				++	++		+			—	++				
8	—	+	+			+++			—	++	++							+++	+					
9	—	—				++			—	+					+++		++						+++	
10	—	—							—	+														

Group II Tissue Reaction in Infected Wounds

Procedure. The procedure employed was essentially similar to that in Group I, except that the sheath and fibers of the rectus muscle were divided down to the peritoneum and 1 cubic centimeter of a 24 hour broth culture of *Bacillus coli* was introduced into the wound before the sutures were applied. Wire sutures were employed to reapproximate the rectus sheath throughout one half of the incision for controls No. C silk was used to close the other half of the rectus sheath in 4 wounds and in another 4 wounds No. 1 chromic catgut was employed. Observations were made, and tissues were removed for microscopic examinations on the 2nd, 5th, 8th, and 14th days after the application of the sutures.

Gross examination. All wounds became swollen after 48 hours and showed signs of mild suppuration during the next few days. By the end of one week, most of the wounds appeared to have healed externally. At the time of removal of the specimens, however from 2 to 3 cubic centimeters of pus was evacuated from each of the 4 and 5 day wounds and from the 8 day wound containing catgut. In 3 other wounds, 1 of 8 days containing silk and the 2 others of 14 days containing silk and catgut, respectively, there was no free fluid. There was surprisingly little reaction around the wire sutures in any of the wounds even when free pus was present. Around the catgut, extensive necrosis and fibrinous exudate were noticed. In the 14 day specimen, the sutures were

partially dissolved and came out on slight manipulation. However in the 8 day specimen, most of the catgut sutures still were intact although surrounded by purulent exudate. An intermediate reaction was seen around the silk sutures. In the 8 and 14 day specimens the wounds were healed and clean. Immediately around the silk, a small amount of mucogelatinous exudate remained.

Microscopic examination. *Wire sutures.* The sutures in the 2 day old wound were surrounded by a small amount of leucocytic and fibrinous exudate which was continuous with a similar exudate present throughout the wound. In the 5 day wound the acute reaction around the sutures had subsided and fibroblasts had appeared, although signs of acute inflammation still were present in the tissues farther removed from the sutures. In the 8 day specimen the sutures were surrounded by a thin layer of hyaline material. The acute inflammatory reaction in the surrounding tissues also had subsided and granulation tissue infiltrated by lymphocytes and plasma cells had appeared. In the 14 day wound the sutures were surrounded by an inner thin layer of hyaline material and an outer fairly broad zone of fibrous tissue.

Silk sutures. In the 2 day wound, the sutures were infiltrated by leucocytes and surrounded by a moderate amount of serofibrinous and leucocytic exudate. In the 5 day wound, the acute inflammatory reaction in the surrounding tissues had become much more extensive. At 8 days,

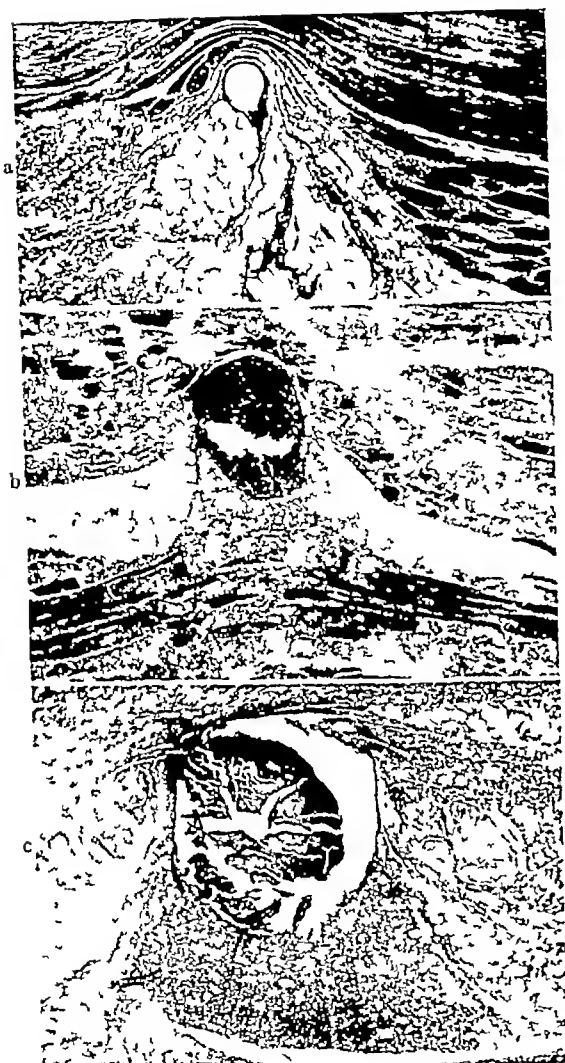


Fig 1 Tissue reaction to sutures, 2 days after application $\times 40$ a, Wire (represented by an oval empty space in all illustrations) Note absence of cellular infiltration around suture and only slight inflammatory reaction in surrounding tissues b, No C silk Suture is partially encircled by purulent exudate with moderate inflammatory reaction in surrounding tissues c, No 1 chromic catgut Very extensive acute inflammatory cellular infiltration



Fig 2 Tissue reaction to sutures, 5 days after application $\times 40$ a, Wire There are a moderate number of fibroblasts around the suture Note the marked constriction on the tissue in this section b, No C silk The acute inflammatory reaction in the surrounding tissues is subsiding, granulation tissue has formed in the surrounding tissues c, No 1 chromic catgut Very extensive purulent exudate still is present

the sutures were surrounded by granulation tissue which was infiltrated chiefly by leucocytes and to a less extent by lymphocytes, plasma cells, and large mononuclear phagocytic cells. In the 14 day specimen extensive granulation tissue had formed and there was very active proliferation of fibroblasts, especially around the sutures. Large numbers of leucocytes still were present, some

of them were among the filaments of silk. A large number of mononuclear phagocytes were scattered among other cells in the granulation tissue, but they did not encroach upon the sutures.

Catgut sutures Sutures in the 2 day wound were surrounded by a large amount of fibrinopurulent exudate which became even more abundant after 5 days. Fragmentation of the

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	Ke	Co	Ke	Co	Ke	Co	Ke	Co	Ke	Co	Ke	Co	Ke	Co	Ke	Co	Ke	Co	Ke	Co	Ke	Co	Ke	Co
Duration of wound—days																								
1	+				+++	++			—				—	—	—	—	—				—	—		
2	±	+++	++			+++			—	—	—		—		—	—	—	—						
3	±				++				—				—								—			
4	±				+++	++			—				+		+	+					—	—	—	—
5	±	+			+++	++			—	+++	++		—	++	++	++	++	+	—	—	—	—	+	—
6	—				++	+		+++	—				++	++	—	+++	+		—	+++		+		—
7	—	±	±		+++				—	++	++			++		+	+++	++					++	
8	—	—				++			—	±				+++		+	++					+++		
9	—	—							—	±						++								

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Duration of wounds—days	Reaction Suture	Acute inflammatory reaction			Granulation tissue			Fibrosis		
		Wire	Silk	Catgut	Wire	Silk	Catgut	Wire	Silk	Catgut
2		+	+++	+++ ++	—	—	—	—	—	—
5		+	+++	+++ ++	—	—	—	+	—	—
8		—	++	++ ++	—	+++	++ ++	+	+	—
14		—	+	++ ++	—	+++	++ ++	+	++	—

where in the wound, the silk and catgut sutures, on the other hand, were surrounded by many more leucocytes. In the wounds of 8 and 14 days (Fig 5 and 6), the difference was even more striking. The inflammatory reaction around the wire sutures had subsided, but the silk and catgut sutures still were bathed by purulent exudate.

Group III Peritoneal Reaction

Procedure Rectus incisions 4 inches in length were made on each side of the midline of the abdominal wall of 4 dogs. The peritoneum was incised along the entire length of each incision, but the structures within the peritoneal cavity were not disturbed. The peritoneum was reapproximated with a continuous suture of No. 1 chromic catgut in the upper half and a continuous suture of No. 35 alloy steel wire in the lower half of the incision on the right side. On the left, a continuous wire suture was employed in the upper half and a continuous suture of No. C silk in the lower half of the incision. The rectus sheath and the skin were closed with interrupted sutures of No. A silk on both sides. These animals were sacrificed 7, 11, 14, and 21 days later, respectively.

Results In the first 3 dogs, identical pictures were observed. In the areas sutured with catgut or silk, the whole line of the peritoneal incision was covered by adherent omentum while the portions sutured with wire were entirely free and were represented by linear scars (Fig 7). In the fourth dog, the segment sutured with silk was covered heavily by omentum while the other three areas all had healed without adhesions.

Group IV Healing of Infected Wounds

Procedure The method used in this series of experiments was similar to that employed by Shambaugh and Dunphy (13) in their study of the relative merits of silk and catgut sutures in infected wounds, except that fine alloy steel wire was used with silk and catgut for controls.

A rectus incision down to but not through the peritoneum was made on each side of the midline of the abdominal wall of a dog. To each of the wounds, 1 cubic centimeter of a saline suspension of dog's feces was applied in order to produce marked infection. On the right side the rectus sheath was closed by means of interrupted sutures of No. 35 alloy steel wire. The same material was used for ligating bleeding points in the wound. On the left side an equal number of interrupted sutures of No. 1 chromic catgut was employed. No. 1 plain catgut was used for ligating bleeders. The skin was closed with interrupted sutures of fine silk on both sides. This procedure was carried out in 2 dogs. In another 2 dogs, a similar procedure was employed except that in the left rectus wound, No. C silk was used for the anterior rectus sheath and No. A silk for ligating bleeding vessels. All the wounds were examined daily. Alternate skin stitches were removed 3 days, and the remaining stitches 5 days, after the operation. When an accumulation of pus was noticed, the wound margins were separated with a clamp and gentle pressure was applied to the rest of the wound in order to evacuate the discharge. No other treatment was given except the application of a sterile dry dressing after each examination.

Results All wounds were swollen and frankly suppurating 48 hours after the operation. The initial swelling was most marked in those wounds closed with catgut, least in those closed with wire, and intermediate in those in which silk had been employed. The amount of pus evacuated on the first separation of the wound corresponded closely to the degree of the swelling. The wounds closed with wire progressed rapidly toward healing as soon as the pus was evacuated. By the end of the first week, all discharge had ceased. All four wounds sutured with wire healed completely by the end of 2 weeks. None of the wire sutures was discharged. The two wounds closed with catgut showed the largest amount of discharge.

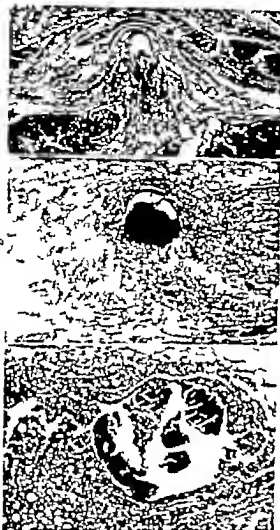


Fig. 3. Tissue reaction to sutures, 9 days after application. $\times 40$. a, Wire. The inflammatory reaction has entirely subsided, slight fibrosis is seen. b, No. C silk. The suture is surrounded by organizing granulation tissue. c, No. chronic catgut. Fragmentation of the suture has occurred. There still is much leucocytic infiltration and granulation tissue.

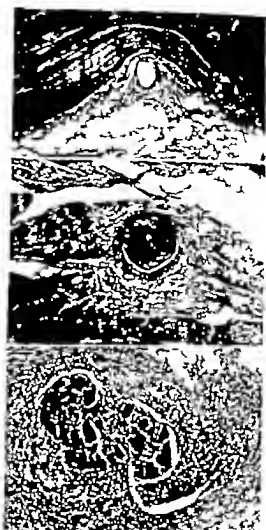


Fig. 4. Tissue reaction to sutures, thirteen days after application. $\times 40$. a, Wire. Very little fibrosis is seen. b, No. Catgut. Moderate fibrosis. c, No. chronic catgut. The suture still is surrounded by granulation tissue. Fibrosis is taking place at the periphery. Note the infiltration of leucocytes between the fragments of the suture.

sutures with penetration of leucocytes was observed in the 5 day specimen. In the 8 day specimen the sutures appeared as fragments in the center of an abscess lined by a wall of granulation tissue heavily infiltrated by leucocytes. Only a few lymphocytes, plasma cells, and large mononuclear phagocytic cells were present. By 14th day picture still was the same, except that there was more fibrosis of the granulation tissue.

Summary The tissue reaction to wire silk, and catgut sutures in infected wounds is summarized in Table II. In the 2 and 5 day specimens, there was a diffuse inflammatory reaction throughout the whole wound as a result of the infection. However the reaction in the immediate neighborhood of the sutures varied according to the suture material. The cellular infiltration around the wires was no heavier than that else-

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2		+	+++	+++ ++	—	—	—	—	—	—
5		+	+++	+++ ++	—	—	—	+	—	—
8		—	++	++ ++	—	+++	++ ++	+	+	—
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Fig. 5. Tissue reaction to sutures in infected wounds, 8 days after application. $\times 40$. a, Wire: The inflammatory reaction has subsided and fibrosis has begun. b, No. C silk: Extensive granulation tissue formation is evident with infiltration of leucocytes around and into the suture. c, No. chronic catgut: The reaction is even more marked than in b, note marked fragmentation of suture.

More than half of the sutures escaped with the pus on the fourth and fifth days. These wounds healed 8 and 10 days, respectively later than those closed with wire (Fig. 8). During the first 2 weeks, the wounds closed with silk progressed better than those closed with catgut, although they showed more swelling and discharge than those in the same animals closed with wire. How-



Fig. 6. Tissue reaction to sutures in infected wounds, fourteen days after application. $\times 40$. a, Wire: Stark fibrosis. b, No. C silk: The suture is surrounded by granulation tissue with marked leucocytic infiltration. c, No. chronic catgut: The suture has been partially absorbed. Extensive granulation tissue and purulent exudate are present.

ever they drained for a longer period of time. After 2 weeks, while the wounds closed with wire in the same dogs had healed completely, discharging sinus persisted in each of the wounds closed with silk (Fig. 9). In one dog the sinus closed spontaneously 16 days later; in the other it persisted for 43 days without sign of healing. When the sinus tract was laid open, it was found t

be lined by soft gelatinous granulation tissue within which were buried five silk sutures. These were removed, and the wound healed 10 days later.

CLINICAL STUDY

During the past year, one of us (Y. K. W.) has used fine alloy steel wire as the main suture material for the closure of 40 abdominal incisions. In each instance the peritoneum was closed with a continuous suture of No. 1 chromic catgut, the anterior rectus sheath was reapproximated with figure-of-eight sutures of No. 35 alloy steel wire, the subcutaneous layer was closed with interrupted sutures of the same material (in thin individuals this layer of sutures was omitted), and the skin was brought together with interrupted sutures of No. A silk. Hemostasis was secured largely by electrocoagulation.

All of the incisions, with three exceptions, were of rectus or paramedian type, varying from 10 to 20 centimeters in length. More than two-thirds of the operations involved the opening of the lumen of the gastrointestinal tract. There were 14 gastrotomies, 1 total and 2 partial gastrectomies, 7 instances of resection and anastomosis of the small or large intestine, 6 operations for intestinal obstruction (enterostomy, colostomy, division of peritoneal adhesions, etc.), 2 instances of simple exploratory celiotomy, and 8 other operations upon the spleen, liver, and biliary tract. Thirty-seven of the 40 wounds were clinically aseptic while 3 were made through contaminated fields. These two groups are considered separately.

Group I Clean Wounds

Two patients of this group did not recover from the operation. However, at the time of death, 1 and 5 days, respectively, after the operation, the wounds showed no sign of infection. The wounds in the other 35 patients healed *per primam*. It was our general impression that the induration along the line of the incision during the course of healing of these wounds was definitely less than that in wounds closed with either catgut or silk. No patient had undue pain or other complaint that could be attributed to the presence of the wires. Even in thin individuals, when the sutures could be palpated through the skin, there was no tenderness. In no instance did a suture work out through the skin during the period (a few weeks to a few months) this group of patients was under observation. Four patients with carcinoma of the esophagus died in the hospital from 1 to 8 months after gastrotomy. Postmortem examination showed that all the wire sutures were well preserved and without evidence of gross change.



Fig. 7. Pentoneal surface of abdominal wall of dog showing parallel rectus incisions closed with continuous sutures of different material: A and D, No. 35 alloy steel wire; B, No. C silk; C, No. 1 chromic catgut. Specimen excised 2 weeks after operation. Note the smooth healing in the sections sutured with wire and the heavy omental adhesions in the sections sutured with catgut or silk.

Microscopic examination of the tissues around the sutures revealed a minimal amount of fibrosis.

The largest group in this series of cases was that of gastrotomy of the Janeway type for patients suffering from carcinoma of the esophagus. It was with the idea of reducing an excessively high incidence of postoperative wound infection in this group of debilitated patients that we first began to employ wire sutures for the closure of the abdominal wound. During the last 4 years, 62 operations of this nature have been performed by 8 surgeons in the Peiping Union Medical College Hospital. The incidence of infection and disruption of the wounds, grouped according to the suture material used for the closure of the abdominal wall, is shown in Table III.

It is not justifiable to draw any conclusion concerning the small group of cases in which catgut was used, although the fact that infection and disruption occurred in 2 of the 3 cases suggests that catgut is an unsuitable suture material. In comparing the incidence of complications in the 2 other groups, there was a marked lowering of the rate of infection in the group in which wire was used, but the incidence of disruption was



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TABLE III—COMPLICATIONS OF ABDOMINAL INCISIONS IN JANEWAY GASTROSTOMIES FOR CARCINOMA OF THE ESOPHAGUS

Type of suture material	Cases	Infection		Disruption	
		Number	Percentage	Number	Percentage
Catgut	3	2	66 7 ± 22 5	2	66 7 ± 22 5
Silk	36	9	25 0 ± 4 9	1	2 8 ± 1 9
Wire	23	2	8 7 ± 4 1	2	8 7 ± 4 1
Whole series	62	13	21 0 ± 3 5	5	8 1 ± 2 3

tion His wound became infected due to necrosis of the gastrostomy stump and ruptured on the seventh postoperative day The other patient developed a tracheoesophageal fistula at the site of the carcinoma Violent attacks of coughing followed and the wound broke open on the eighth postoperative day

Since factors other than the type of suture material employed must be considered in the problem of the healing of wounds, it may be worthwhile to compare the incidence of complications following the same type of operation performed by the same operator The personal series of Janeway gastrostomies for carcinoma of the esophagus of one of us (Y K W) consists of 22 operations One of 2 wounds closed by catgut became infected and disruption followed, 2 of 7 wounds closed by silk became infected, with disruption in 1, but all of 13 wounds closed by wire healed without complication

Group II Contaminated Wounds

In 3 of the 40 cases in this series, the wounds were contaminated grossly at the time of operation

CASE 1 In an infant 6 months of age, excision of a congenital umbilical fistula due to a patent omphalomesenteric duct was carried out The incision was made through the macerated skin around the umbilicus The wound was closed with wire sutures and healed without sign of infection

CASE 2 In performing a splenectomy for cirrhosis of the liver, it became necessary to extend the incision through an infected area of the abdominal wall On the sixth day, a localized abscess was found beneath the skin at the site of the original incision Following separation of the edges of the wound in this area the infection subsided promptly Complete healing occurred within 2 weeks

CASE 3 During an operation for the repair of a fecal fistula, the wound was contaminated by the unexpected opening of a peritoneal abscess The main portion of the wound was closed with wire sutures, but the end overlying the abscess was left open for drainage In spite of the poor general condition and marked nutritional disturbance of the patient, the sutured portion of the wound healed promptly and the whole wound closed by the 28th postoperative day It was not necessary to remove any of the wire sutures during the healing of the wound, nor were any of these sutures extruded spontaneously



Fig 10 Diagram showing the correct, a, left, and incorrect, b, method of twisting the wire sutures

In several other instances in this clinic contaminated wounds closed with fine alloy steel wire (by other surgeons) showed a similar favorable response The wounds either healed without clinical evidence of infection or only mild infection developed Even in the presence of frank suppuration, the wire sutures remained in position and became covered by healthy granulations within a relatively short period of time

FIXATION OF WIRE SUTURES BY TWISTING

The chief objection to the use of alloy steel wire sutures is the difficulty of handling and tying the wire In order to simplify this procedure, we merely twisted the ends of the wire three complete turns instead of attempting to form the usual type of knot Sometimes the twisted ends (which were 2 to 3 mm in length) were turned downward with a hemostat By this method, we not only could anchor the individual sutures in a much shorter period of time, but also could regulate the tension of the sutures more accurately than by the classical formation of knots The last mentioned point constitutes an important reason for the use of this method of fixation of the wire sutures It is imperative, however, that the two ends of the wire be twisted equally so that they will lock and maintain their position (Fig 10)

This method of fixing the wire sutures was used in most of the experimental animals None of the sutures was found to have become untwisted or to have shifted from its original site at the time at which the specimen was removed The method also was employed in 10 patients All wounds healed without complication In 7 instances in which subsequent roentgenological examination was carried out, the wire sutures were found to be in satisfactory position

EVALUATION OF STUDY

We believe that this study has demonstrated a less severe reaction of the body tissues to fine alloy steel wire sutures than to either catgut or silk, under both septic and aseptic conditions The evidence presented by the illustrations alone (Figs 1 to 9) is so striking that further comment scarcely seems to be necessary However, we may summarize our observations in the following manner Fine alloy steel wire sutures initiate only a very mild inflammatory reaction in the surrounding tissues Even this reaction



Fig. 8. Abdominal wounds infected with saline suspension of dogs' feces. The rectus sheath has been closed with No. 35 alloy steel wire on the right side and No. 3 chromic catgut on the left side. a, 3 days after operation. Wire wound, slightly swollen. Less than cubic centimeters of pus evacuated. Catgut wound, markedly swollen 50 cubic centimeters of pus evacuated. b, 5 days after operation. Wire wound, healing; discharge scanty. Catgut wound, still swollen with moderate amount of pus. c, 14 days after operation. Wire wound, almost completely healed. Catgut wound, still discharging pus. Whole incision is uninfected. Complete healing, 21 days later.

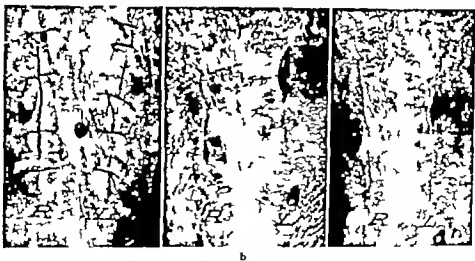


Fig. 9. Abdominal wounds infected with saline suspension of dogs' feces. The rectus sheath has been closed with No. 35 alloy steel wire on the right side and No. 3 silk on the left side. a, 3 days after operation. Wire wound, moderately swollen, 5 cubic centimeters of pus evacuated. Silk wound, markedly swollen 10 cubic centimeters of pus evacuated. b, 5 days after operation. Wire wound, healing, except for superficial necrosis; discharge scanty. Silk wound, moderately swollen with purulent discharge. c, 14 days after operation. Wire wound, completely healed. Silk wound, upper two-thirds of wound uninfected. Wound drained for 45 days and healed only after it was reopened and some silk sutures removed.

distinctly higher in this group than in the group in which the wound was closed with silk. However, in the 2 instances in which disruption of the

wound occurred following closure by wire, the patients suffered from severe attacks of coughing. One developed bronchopneumonia after opera-

PERITONEAL ASPIRATION IN THE DIAGNOSIS OF STRANGULATED BOWEL

FREDERICK C HILL, M D , F A C S , BERNARD J O'LOUGHLIN, B S , and
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DURING the course of some experiments on dogs in which a loop of strangulated bowel was placed in a rubber bag, we observed that within a few hours the bag began to fill with an exudate, profuse in amount, which had a cherry-red or pink color. This fluid appeared before the loop ruptured and the redness of its color gradually increased until after the loop ruptured, when it of course, took on the appearance of the contents of strangulated bowel. We showed in the previous investigations (3) that this fluid is toxic when injected intravenously into another animal. In order to confirm the presence of this exudate, in the absence of the rubber bag although it has been previously mentioned by Scott and Wangensteen who studied the fluid found in various types of obstructions in dogs, we produced strangulated loops of bowel 4 inches long in another series of dogs. We found that fluid which was exactly similar to the fluid present in the bag formed in the abdominal cavity in these animals. The fluid contains blood, and the erythrocytes are present in approximately the concentration which is produced when one drop of blood is placed in one cubic centimeter of water.

Richardson in 1920 called attention to this rusty, blood-stained fluid in cases of strangulation of the bowel and suggested that the appearance of such peritoneal fluid might aid in the diagnosis of intestinal obstruction after the abdomen had been opened. In a series of 135 cases of intestinal obstruction he found 21 in which there were strangulation of the bowel and this typical fluid. There were also a few cases in which, although there was interference with the mesenteric circulation, it was definitely stated that there was no rusty fluid. Richardson believed that these cases came to operation before the fluid had time to form. In some cases of simple obstruction he noted that clear, straw-colored fluid may be present. Scott and Wangensteen in their studies on various types of obstructions in dogs found that when the mesenteric veins were ligated, 50 to 250 cubic centimeters of hemorrhagic fluid having low pro-

tein content and little if any odor, developed. In those dogs with arterial or with both venous and arterial obstruction, 100 to 500 cubic centimeters of dark bloody foul-smelling fluid with high protein content was present.

Because of the striking character of this fluid and its positively diagnostic nature when present, we were led to perform a series of experiments on dogs in which we attempted to aspirate fluid from the abdominal cavity at various intervals after strangulation obstruction had been produced. The procedures followed were the same on 4 animals. Under intratracheal ether anesthesia and with the usual sterile precautions, a midline incision was made, and a segment of jejunum 4 inches long and 1 foot below the ligament of Treitz was ligated with cotton tape. The vessels of the mesentery were included in the ligature but the tape was not pulled tightly enough to obstruct the arteries. The abdomen was then closed in layers by the usual method. The peritoneal cavity was aspirated, a lumbar puncture needle being used at 1, 2, 4, and 6 hour intervals after the operation.

As shown in the accompanying table, in 2 dogs fluid obtained 1 hour after operation contained in one instance many red blood cells and white blood cells, and in the other, white blood cells only. At 2 hours, in 3 of 4 animals, fluid was obtained which under the microscope showed many red blood cells and white blood cells. Culture of this fluid showed no growth in one, and showed chain streptococci and gram negative short rods in another. At 4 hours, aspiration of the abdominal cavity of all 4 animals revealed typical reddish fluid which was diagnostic of strangulation and culture from this time on was always positive for bacteria which we did not identify. At 6 hours, in all animals, the same type of fluid was obtained. The animals died during the night, and in all cases the loop was found at necropsy to be ruptured. Two additional dogs were operated on and obstructed loops 2 feet in length were produced. These dogs were sacrificed at 14 to 24 hours, and the loops of bowel were found not to be ruptured. In each case about 40 cubic centimeters of the typical fluid was found in the pe-

From the Department of Surgery Creighton University School of Medicine.

seems more likely to be due to trauma incidental to the passage of the needle and the suture than to the continued presence of the wire. This reaction soon subsides and is replaced by the healing process. In the instance of silk, the initial reaction is distinctly more marked and the subsequent fibrosis also is relatively more extensive. In infected wounds leucocytes and granulation tissue not only appear around the sutures but also infiltrate between the filaments of the silk. Therefore until the sutures are removed the infection is likely to persist. As Meade Jackson and Ochsner have pointed out, this is the chief reason why the presence of silk sutures may seriously delay the healing of infected wounds. Catgut sutures produce the most extensive early as well as delayed type of inflammatory reaction. As a matter of fact, a majority of all catgut sutures actually lie bathed in minute aseptic abscesses until their filaments are largely or completely absorbed. These changes certainly predispose toward infection of the wound. Furthermore, in the presence of infection, catgut sutures either are dissolved or sloughed off before solid healing of the wound has had time to occur. This leads to disruption of the wound in certain instances.

From these observations, it may be suggested that catgut is not a suitable suture material for the closure of either aseptic or infected wounds. Silk is a generally satisfactory material for clean wounds, but is to be avoided in the presence of infection. Fine alloy steel wire is preferable to either catgut or silk for both clean and infected wounds. We believe this type of wire to be especially suitable for the closure of abdominal wounds after operations in which there is a potential chance of contamination, as in extensive resections or anastomoses of gastrointestinal tract. In presence of frank infection, fine alloy steel wire is undoubtedly the suture material of choice.

In using wire sutures, the general principles laid down by Halsted for the use of silk should be rigidly observed, with special emphasis on the avoidance of tension. In our experience No. 35 alloy steel wire is satisfactory for suturing both the aponeurosis and the subcutaneous fascia. Thicker and stronger wire is probably unnecessary. The wire can be sterilized by boiling or autoclaving. It may be sterilized repeatedly without loss of strength. The low cost of the wire (a) is another distinct advantage.

SUMMARY AND CONCLUSIONS

1. The behavior of fine alloy steel wire sutures was studied in dogs, catgut and silk sutures being

used as controls. Gross and microscopic observations were made in both aseptic and infected wounds. It was found that wire sutures produced the least amount of tissue reaction and promoted the most rapid healing of the wounds.

2. Clinical experience with forty abdominal incisions closed by fine alloy steel wire sutures showed that all clean wounds healed *per primam*. Reduction in the incidence of wound infection was especially remarkable in a group of January gastrostomies established for patients suffering from carcinoma of the esophagus. In 3 instances of contaminated wounds, primary healing occurred in 1 and only localized infection developed in the others, both of which healed without disruption and without extrusion of the suture material.

3. On the basis of these observations, more extensive use of fine alloy steel wire sutures is recommended, especially in wounds potentially or obviously contaminated. We realize, however, that the final evaluation of this type of suture can be determined only by careful observation of the immediate as well as the late results in a much larger number of cases.

4. In using wire sutures, the rules laid down by Halsted for the use of silk should be followed closely. Special emphasis should be placed on the avoidance of tension when the sutures are tied. The fine caliber and the unyielding character of the wire tend to cause it to constrict and to cut through the tissues if this precaution is not observed.

5. In order to facilitate the tying of wire sutures and the regulation of the tension exerted by them on the tissues within their grasp, we recommend elimination of the customary knot and fixation of these sutures by simple twisting of the ends of the wire for three complete turns.

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PERITONEAL ASPIRATION IN THE DIAGNOSIS OF STRANGULATED BOWEL

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DURING the course of some experiments on dogs in which a loop of strangulated bowel was placed in a rubber bag, we observed that within a few hours the bag began to fill with an exudate, profuse in amount, which had a cherry-red or pink color. This fluid appeared before the loop ruptured and the redness of its color gradually increased until after the loop ruptured, when it of course, took on the appearance of the contents of strangulated bowel. We showed in the previous investigations (3) that this fluid is toxic when injected intravenously into another animal. In order to confirm the presence of this exudate, in the absence of the rubber bag although it has been previously mentioned by Scott and Wangenstein who studied the fluid found in various types of obstructions in dogs, we produced strangulated loops of bowel 4 inches long in another series of dogs. We found that fluid which was exactly similar to the fluid present in the bag formed in the abdominal cavity in these animals. The fluid contains blood, and the erythrocytes are present in approximately the concentration which is produced when one drop of blood is placed in one cubic centimeter of water.

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tein content and little if any odor, developed. In those dogs with arterial or with both venous and arterial obstruction, 100 to 500 cubic centimeters of dark bloody foul-smelling fluid with high protein content was present.

Because of the striking character of this fluid and its positively diagnostic nature when present, we were led to perform a series of experiments on dogs in which we attempted to aspirate fluid from the abdominal cavity at various intervals after a strangulation obstruction had been produced. The procedures followed were the same on all animals. Under intratracheal ether anesthesia, and with the usual sterile precautions, a midline incision was made, and a segment of jejunum 4 inches long and 1 foot below the ligament of Treitz was ligated with cotton tape. The vessels of the mesentery were included in the ligature but the tape was not pulled tightly enough to obstruct the arteries. The abdomen was then closed in layers by the usual method. The peritoneal cavity was aspirated, a lumbar puncture needle being used at 1, 2, 4, and 6 hour intervals after the operation.

As shown in the accompanying table, in 2 dogs fluid obtained 1 hour after operation contained in one instance many red blood cells and white blood cells, and in the other, white blood cells only. At 2 hours, in 3 of 4 animals, fluid was obtained which under the microscope showed many red blood cells and white blood cells. Culture of this fluid showed no growth in one, and short chain streptococci and gram negative short rods in another. At 4 hours, aspiration of the abdominal cavity of all 4 animals revealed typical reddish fluid which was diagnostic of strangulation, and culture from this time on was always positive for bacteria which we did not identify. At 6 hours, in all animals, the same type of fluid was obtained. The animals died during the night, and in all cases the loop was found at necropsy to be ruptured. Two additional dogs were operated on and obstructed loops 2 feet in length were produced. These dogs were sacrificed at 14 to 18 hours, and the loops of bowel were found not to be ruptured. In each case about 40 cubic centimeters of the typical fluid was found in the peri-

FOUR INCH STRANGULATED LOOPS

Dog no. Weight in lbs.	Hours after obstruction	Amount of aspirated fluid	Color of fluid	Source of exudate	Culture of exudate	Autopsy findings
147		drop	Clear	Few RBC; many WBC	Negative	Loop ruptured and part missing; peritoneal fluid present. Loop black. Omentum and mesentery torn together with ad- hesions
		drops	Rusty	Many RBC, WBC and large fat globules	Aerobic: few short chains streptococci Slight acid Anaerobic: few gram negative short rods	
	6	c.c.	Rusty	Same as above	Aerobic, acid, no gas; morphology as above Anaerobic: pollicle forming gram negative short rods and short chains streptococci	
152		None				Loop ruptured and near missing; fluid present. No adhesions
		drop	Rusty	WBC		
	6	3 drops	Rusty	RBC and WBC	Aerobic: acid, no gas Anaerobic: pollicle formed	
153 20		drop	Clear	WBC		Ruptured loop, near per- itoneal fluid, very thin
		drop	Rusty	WBC many RBC		
		drop	Rusty	WBC and RBC		
	6	3 drops	Rusty	WBC with few in- transmissible bacteria and many RBC	Aerobic: gram positive and gram negative short rods, many short chains streptococci, acid forming	
154 22		drop	Clear	Many RBC and WBC		Ruptured loop same as above
		10 drops	Rusty	Many RBC and WBC	Aerobic: short chains streptococci Anaerobic: gram negative short rods	
		drop	Rusty	WBC—very poly- morphous RBC	Aerobic: streptococci, streptococci, gram negative rods Anaerobic: short chain streptococci, gram positive rods	
	6	6 drops	Rusty	Same as above	Aerobic: acid-forming short gram negative rods, short chain streptococci Anaerobic: same as above	

toneal cavity. Samples of this fluid were removed for culture and smear and the findings agreed with those of the fourth and sixth hour punctures, but the quantity of organisms and cellular matter was much greater. In no instance, as far as we were able to determine, was the bowel punctured by the aspirating needle. As control experiments, a simple obstruction was produced by a tape in 2 other dogs and 18 hours later no fluid was found on opening the peritoneal cavity.

Denzer (12) and Neuhauf and Cohen have previously reported on the value of peritoneal aspiration in the clinical diagnosis of various types of peritonitis, and all emphasize the safety of the procedure and point out the difficulty of puncturing the intestine. The bowel moves away from the point of the needle and it takes considerable force to enter into its lumen. If the bowel should happen to be adherent to the peritoneal wall at the site of the puncture, the intestine probably would be penetrated, but under these conditions

the puncture would be of little importance since there would be no leakage into the peritoneal cavity. The site chosen for puncture is probably of little importance. If a mass is present it should be avoided and the needle, of course, should be inserted high enough above the symphysis to miss the bladder. We have performed aspiration on one patient with acute intestinal obstruction and considerable distention, and no puncture of the intestine occurred. It is not difficult to tell when the needle enters the peritoneal cavity and with ordinary care we believe that the procedure is safe. It sometimes requires aspiration for as long as a minute to obtain the fluid, according to Denzer and if no leakage of air into the peritoneal cavity is permitted before suction is applied, it is easier to aspirate the fluid. We are not reviewing the value of this procedure in the diagnosis of other intra-abdominal conditions, because Horsley and the authors previously quoted have already done so.

CONCLUSION

In the experimental animal, strangulated bowel can be diagnosed within 4 hours after onset by the aspiration of characteristic fluid from the abdominal cavity

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EDEMA OF THE PANCREAS

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EDEMA of the pancreas has been described first by Archibald, and several years later as a clinical entity, by Zoepffel. The cause and nature of the edema is still obscure. Some authors believe it is not related to pancreatitis but is a disease by itself, due to inflammation or to retention of the pancreatic secretion in the ducts. Other authors consider it to be the precursor or a mild manifestation of pancreatitis or pancreatic necrosis. The appearance of an edematous pancreas gives the impression that one is not dealing with an edema as seen in inflammation or congestion of other organs. This is probably the reason why this process has not been called simply edema of the pancreas, but usually is called "glassy edema of the pancreas." Cutting into such an edematous organ reveals that the edematous appearance is due to a gelatinous imbibition of the tissues, which do not contain much free fluid, no free fluid is oozing from the cut surface of the edematous pancreas as seen in edema of other organs. A small quantity of free fluid accumulates, however, under the capsule and in the interlobular spaces of the pancreas, which can be aspirated for chemical determinations. In cases of edema of the pancreas in dogs as well as in humans just as in cases of acute pancreatitis, exudate is found in the peritoneal cavity containing a high concentration of pancreatic enzymes. (2) These enzymes are undoubtedly derived from the pancreas. In animal experiments direct observation of the initial stages of pancreatic edema shows the exudation of fluid from the surface of the gland. These findings suggest that in edema of the pancreas (as in pancreatitis) a diffusion of pancreatic juice occurs first into the pancreatic

parenchyma and later into the peritoneal cavity. In recently published animal experiments it has been shown that this subcapsular and interstitial edema fluid contains large amounts of pancreatic enzymes (2). It was concluded from this finding that edema of the pancreas is due to an imbibition of the pancreatic and peripancreatic tissues with pancreatic juice.

It is well known that ligation of the main or of all of the pancreatic ducts in dogs usually is not followed by edema of the pancreas. Injection of bile, duodenal juice, or other substances into one pancreatic duct followed by ligation of the duct, however, leads regularly to an edema of the organ within a few minutes. In order to find out whether edema of the pancreas could be produced by more or less physiological means, that is, by stimulating the gland while one or more ducts were obstructed, the following experiments were performed.

In 4 dogs, the main pancreatic duct and, in 2 dogs, the main and one accessory duct were ligated. The pancreas was observed 5 to 60 minutes after this procedure, and no edema was observed. At that time 3 to 4 milligrams per kilogram of body weight of secretin were injected intravenously, and within a few minutes (3 to 5) edema of the pancreas began to appear, spreading rapidly over the entire organ. Fifteen to 30 minutes later the entire pancreas had been involved extensively. The edema subsisted for a number of hours, then it subsided gradually and had disappeared almost completely 4 hours after injection. At that time a few fat necroses could be observed in the peripancreatic tissue of a few dogs. Some subcapsular edema fluid was aspirated at the height of the edema and was found to contain large amounts of amylase and lipase, similar to edema fluid obtained following injection of bile into the pancreas (2).

From the Department of Gastro-Intestinal Research, Michael Reese Hospital, Chicago. Aided by the A. B. Kuppenheimer Fund. A preliminary report read at the meeting of the American Physiological Society, April 1941.

Peritoneal exudate was usually found as early as 15 minutes after administration of the secretin and likewise showed a high concentration of amylase and lipase. The increase of blood enzymes which is regularly observed after ligation of pancreatic ducts occurred much later than the finding of enzyme containing fluid in the peritoneal cavity.

In a control experiment the pancreatic duct was not ligated and secretin was injected intravenously. No change in the pancreas occurred within 1 hour, when the main pancreatic duct was ligated and the same amount of secretin was injected as before. A few minutes later an extensive edema of the pancreas developed.

In 4 dogs the main pancreatic duct was ligated and drugs which are known to stimulate pancreatic secretion like mecholyl and eserine or pilocarpine were injected. This procedure was not followed by edema of the pancreas. In 1 dog .05 cubic centimeter of its own duodenal juice was injected into the main pancreatic duct, which was then ligated. Ten minutes later no change was noted. After that pilocarpine was injected subcutaneously and a few minutes later extensive edema of the pancreas developed.

Finally in 1 dog both pancreatic ducts were ligated and one tenth normal hydrochloric acid solution was infused into the duodenum at the rate of 40 drops per minute. Fifteen minutes after the beginning of the infusion of hydrochloric acid into the duodenum a marked edema of the pancreas developed in the central portion of the organ. The edema was not as extensive, however as the one observed following injection of secretin. It is apparent that in this experiment the edema of the pancreas was produced by secretin liberated by the hydrochloric acid from the mucous membrane of the small intestine.

These experiments demonstrate that in the presence of complete or partial obstruction to the outflow of pancreatic juice an edema of the pancreas may be produced in dogs by injection of secretin or by the physiological mechanism of liberation of secretin in the small intestines, after acid gastric juice has entered the latter. The secretory effect of secretin is much greater than

that of the vagotropic drugs applied, namely pilocarpine and mecholyl and eserine. It is possible that the production of edema of the pancreas in case of retention of secretion is dependent on the amount of secretion retained, in other words, on the degree of pressure developed within the ducts. However the different composition of pancreatic juice secreted to secretin and to vagotropic drugs must be considered also. The experiment in which injection of a very small amount of duodenal juice into a pancreatic duct was not followed by edema but in which, following injection of pilocarpine edema developed points to an activation and potentiation of pancreatic enzymes within the duct system of the pancreas.

Our observations on dogs may be applied to man. It is a well known clinical observation that attacks of pancreatitis usually begin after a copious meal. If in such a person the outflow of pancreatic juice would be obstructed more or less completely even for a very short period of time, the secretin mechanism activated by the hydrochloric acid from the stomach as well as by products of digestion would be sufficient to produce an acute edema of the pancreas.

SUMMARY

Pancreatic edema is produced by the diffusion of pancreatic juice into the pancreatic parenchyma and peripancreatic tissues. Extensive edema of the pancreas could be produced in animal experiments by ligation of a pancreatic duct and subsequent stimulation of pancreatic secretion by secretin, or by activation of the secretin mechanism by infusion of dilute hydrochloric acid into the duodenum. Under the same conditions stimulation of pancreatic secretion by vagotropic drugs did not lead to formation of edema.

These experiences may be applied to man in whom, under conditions of complete or incomplete obstruction of the pancreatic duct, the secretin mechanism activated by a meal may cause edema of the pancreas.

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CHANGING CONCEPTS OF THE ACCEPTED TREATMENT FOR ACUTE HEMATOGENOUS OSTEOMYELITIS

TEN years ago in most medical schools acute hematogenous osteomyelitis was considered an excellent example of acute infectious surgical disease. The necessity of making an extremely early diagnosis was emphasized, successful treatment was thought to be contingent entirely upon this. The treatment, almost the entire treatment, was then based upon drilling into the bone, the intention being to permit the escape of the infection. In 1920, the second edition of one popular textbook of surgery expressed this dominant idea, thus "As soon as the diagnosis is made the bone should be opened. Delay even of a few hours is dangerous."

Acute hematogenous osteomyelitis is not a particularly common disease, a fact which may explain the now seemingly long delay in questioning whether the method of treatment being taught was the best form of manage-

ment even for a decade ago. A real reckoning of the question revealed surprising figures. For example, in the Charity Hospital at New Orleans, from 1930 to 1936, inclusive, there were 112 primary cases of acute hematogenous osteomyelitis, that is, cases in which patients had not been operated upon elsewhere and not recurrent cases. In this group the accepted teaching that drilling the bone was the essential part of treatment was followed, in 84.8 per cent of the cases the initial operation involved opening the bone. Operation was performed in over 71.4 per cent of the cases within 48 hours after patients were admitted to the hospital and in 90 per cent of these the bone was opened. Thus in 64.3 per cent of all the cases the bone was opened within 48 hours after the patient entered the hospital. The surprising mortality for the entire series was 26.2 per cent, and for those operated upon within 48 hours after admission to the hospital, 32.2 per cent. Obviously something was wrong. This and many other analogous reports showed that operation was not accomplishing what surgical teaching maintained it would. From 1927 through 1940, 66 patients with primary acute hematogenous osteomyelitis have been admitted to Charity Hospital. In this group is reflected a much more conservative attitude regarding operation, for 36.4 per cent of the patients were operated upon during the first 48 hours after entrance to hospital but in only 27.3 per cent of the 66 patients was operation involving the opening into a bone done within the first 48 hours after entrance. Only 4 patients died in this group of 66, thus giving a mortality of 6 per cent in stark contrast to the mortality of the previous series.

Even though these figures cover a period in which there was a changing attitude regarding operation early in the presence of acute osteomyelitis, and even though they indicate that the mortality rate fell when fewer operations on the bone were performed in such cases, they do not prove conclusively that operation early in osteomyelitis is deleterious. Operation may not have been the only factor in the improved mortality. Even those of us who are convinced, upon present evidence, that operation is harmful early in the disease are justified to the extent only of keeping an open mind. The improvement in mortality certainly is not due to more operations or to earlier operation. It may be due largely to factors other than operation. The correct answer to the question whether or not operation is of benefit early for acute hematogenous osteomyelitis may change the mortality rate as little as 1 or 2 per cent in a series of one hundred cases, for the reason that much improvement has followed the use of more recent therapeutic measures. During recent years, particularly in the treatment of other surgical conditions, the profession has had an impressive lesson on the dangers of dehydration and changes in the blood chemistry in sick surgical patients, with the result that whether emphasized in case reports or not, patients undoubtedly now receive more careful attention as to maintenance of normal fluid and electrolytic balance. Moreover in recent years the repeated re-emphasis of the necessity of maintaining protein requirements has led to the more frequent administration of transfusions. Immunological benefits have resulted from these transfusions. The basic physiology of the patient is thus kept more nearly normal so that his intrinsic defenses against infection are thereby supported. Moreover extrinsic factors, such as chemotherapy and antitoxin, have been

proved of unquestioned value in the management of the condition and though it seems a simple procedure and its effect almost incredible, absolute immobilization of the affected extremity appears to be remarkably beneficial.

Such acknowledged therapeutic advances must be taken into consideration in evaluating the results of operation in any stage of the disease. The real status of operation—its relative worth in combatting the disease and its comparative value in relation to other measures—is at present, to say the least, controversial. For that reason all suggestive real proof is desirable. Studies should be made of small and of large series of cases not only in relation to the status of operation but also in reference to details in clinical and experimental investigation relating to each therapeutic measure. Chemotherapy and antitoxin likely may prove the most remarkable advances in the management of the disease. Pure controversy will carry little weight in ultimate well founded conclusions. Arguments based on the long accepted concept of the pathogenesis—that the disease begins in the end arteries of the metaphysis that put under pressure comes to the surface through havarian canals and raises the periosteum for variable distances causing sequestration of the underlying bone—may be worthless, for that concept may be wrong. Thrombosis of the nutrient artery may be the most important change in the local pathological process responsible for determining the extent of sequestration. Many points about the disease remain unanswered. It is not common and intensive studies must be made to prove the value of operation and the best methods of management. One point seems well assured and that is that operation alone early in the disease is not the powerful life saving measure that surgical texts and the teachings of 50 years ago indicated. Other measures now

seem as important, or more important, than surgery. The value of operation on the bone early in the disease still remains an unsettled question.

HOWARD MAHORNER

ACUTE CHOLECYSTITIS WITH PERFORATION

HOW frequently is perforation a complication of the acutely inflamed gall bladder? This question is not readily answered if one includes all of those cases in which slightly bile stained fluid, or secondary abscesses are added to a lesser number in which, due to perforation, a diffuse biliary peritonitis is observed.

Acute cholecystitis manifests itself in two distinct clinical types. First, the usually observed progressive condition which requires several days to reach its peak of severity, both as to symptoms and extent of pathology, but which responds to conservative treatment and can be safely carried over the "waiting" period, second, the fulminating type, the symptoms of which are of short duration, very severe, and in which gangrene and perforation are early complications. In the former group the inflammatory process is rather slow. Peritoneal reaction follows a permeation of the gall-bladder wall by infection or the extension of inflammation, adhesions to the liver, duodenum, colon, stomach, and omentum follow, and secondary abscesses are encountered. Less frequently, due to fixation of the gall bladder to the stomach, duodenum, or colon, fistulas develop, anastomosing the gall bladder to one of these hollow viscera. In either event, this process has occurred rather slowly and therefore the peritoneum has been secured against an escape of bile. During this period the cystic duct quite likely has been occluded by a stone within, or by the inflammatory process, and bile is no longer flowing

into the gall bladder so that should perforation occur, there is not an abundance of bile to escape from the gall bladder. However during this time the inflammatory process is likely to spread throughout the biliary ducts and through them or the accompanying lymphatics into the pancreas or liver.

It is in this group of cases that the numerous complications, so much to be feared, are so frequently encountered. It also contributes tremendously to both the morbidity and mortality of gall-bladder disease. Since the progress of the pathology in this group of cases can be measured in days, there is no reason why these patients should not be studied very thoroughly. No factor influencing the element of safety should be overlooked. All of the known laboratory tests which may be used to estimate liver and kidney function and damage should be employed. The degree of jaundice, if any, should be estimated and what effect it has had on bleeding and clotting time known.

These tests can be applied very rapidly. During the period of investigation the patient should receive an abundance of glucose intravenously. No sedatives should be administered and the clinician should make abdominal examinations at frequent intervals.

The fulminating type presents quite a different problem, here as in the first group, history of previously existing gall-bladder disease can be obtained in a majority of the cases, but the onset of the present attack is very sudden. Pain in the upper right abdomen is extremely violent, vomiting is frequently severe, muscle rigidity in the upper right quadrant is pronounced and exquisite peritoneal tenderness is indicated by the slightest pressure on the abdominal wall. The patient usually has some elevation of temperature and the blood count is variously affected. Under the influence of intravenous

fluids the patient's general condition appears improved but abdominal examinations reveal the same exquisite peritoneal sensitiveness as when first observed or possibly it has spread and increased. This clinical condition suggests a perforating or perforated gall bladder. It has been observed in 10.83 per cent of cases of acute cholecystitis.

The mortality in this group of cases is dependent almost entirely upon the length of time existing after perforation and before operation. It is 16.66 per cent. This may be reduced by earlier operation.

A survey of most of the literature of the past ten years on acute cholecystitis indicates the trend of surgeons of today toward earlier operations for this condition.

The mortality in acute appendicitis was gradually lowered, largely by earlier operation, and the mortality and morbidity of perforated gastric and duodenal ulcers have been greatly reduced by similar efforts.

Likewise in considering acute cholecystitis,

surgeons in general would do well if they realized that early operation will do more to reduce both the morbidity and the mortality in this disease than any other treatment, and that while laboratory tests are of incalculable value they must not supplant careful clinical observations for by this latter test must the diagnosis of peritoneal soiling or threatened soiling be made. It is impossible to differentiate a threatened perforation from one that has recently occurred, except by laparotomy.

A biliary peritonitis is known to be highly toxic and fatal in a short time unless adequately interrupted very soon after it has developed.

These facts support the contention that acute cholecystitis with perforation constitutes an abdominal emergency requiring immediate laparotomy and that the complications of the less rapidly developing cases are of such magnitude that the prevention of them by early operation demands very serious consideration.

CHARLES R. EDWARDS.

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AN EXPERIMENTAL STUDY OF URETEROINTESTINAL IMPLANTATION

V The Destiny of the Implanted Ureter

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EXPERIMENTAL investigation has yielded abundant proof that the lower portion of the implanted ureter constitutes an area of crucial importance in determining the success or failure of a ureterointestinal anastomosis. At successive stages following implantation of the dog's ureter by various modifications of the submucosal method, the animals either died or were killed and the intraluminal and intramural segments were subjected to a special study. In addition to gross and microscopic examination, the ureters in several specimens were injected with a 20 per cent suspension of India ink in gelatin and the region of the anastomosis was cleared by the Spalteholz-Skarda technique in order to localize areas of constriction or dilatation. These findings were correlated with the changes reflected in the upper urinary tract.

It was observed that healing at the site of the anastomosis takes place either by primary union and early epithelization or, in the presence of infection, by granulation, cicatrization and late epithelization (Table I). Al-

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though pure forms of both processes occur, the two are more usually associated in one of an innumerable number of possible relationships.

Immediately following operation the usual traumatic manifestations make their appearance. There is edema of the operative area with an infiltration of lymphocytes and plasma cells. Areas of hemorrhage may be present (Fig. 1). A foreign body reaction is observed in the region of the sutures.

If there is no infection or if only a mild degree of infection supervenes, as commonly observed in ureterovesical reimplantation, this reaction rapidly subsides and healing occurs by primary intention (Fig. 2). This is usually achieved by the sloughing of the intraluminal segment of the ureter. Only in rare instances is the length of this segment preserved exactly as introduced at operation. Most frequently a variable portion of the end separates so that the new orifice is in the plane of the mucosa of the implanted viscus or is situated on a low papilla.

In the absence of infection, sloughing is caused by anemic necrosis alone. The reaction is admirably demonstrated in a series of experiments in which a hollow catgut cylinder

TABLE I—FORMS OF HEALING FOLLOWING URETERAL IMPLANTATION

I Early traumatic edema causing variable degrees of ureteral obstruction	
II Without Infection Healing by primary union Early cystic degeneration	II With Infection Infectious, acute, subacute to chronic. Early obstruction of the ureter. Healing by granulation
III Healing completed without constrictions. Final relief of temporary obstruction (The end of the ureter may show least scarred increase)	III Cicatrization. Formation of scar tissue may give rise to late obstructions of the ureter. Late epithelization (The end of the ureter may show less infection + granulation)

was placed in the lumen of the end of the ureter in an attempt to assure the patency of the anastomosis. Since the cylinders fit snugly in many instances with the occurrence of edema, the blood vessels became obliterated and necrosis from pressure ensued (Fig. 3).

If healing takes place by primary union there is little constriction of the ureter other than that occasioned by the transient operative edema. Free communication as demonstrated by injections of gelatin is illustrated in Figures 4 and 5. In addition to exemplifying the ideal which is striven for in all implantations these models serve for comparison with specimens showing obstruction.

When a severe degree of infection ensues an entirely different picture is presented. Soon after the onset of edema the entire wall of the redundant end of ureter becomes engorged with leucocytes chiefly of the polymorphonuclear strain. The adventitia is invaded first but the process soon spreads through the muscularis, the submucosa, and to a lesser degree into the mucosa. The surface of the stump is encased in an inflammatory debris containing conglomerations of bacteria (Fig. 6). The more fulminating the inflammatory reaction, the greater is the tendency to occlude the lumen of the ureter. Granulation tissue makes its appearance and gradually replaces the exudate. New capillaries are formed and, as they grow into the granulations, fibroblasts appear (Fig. 6 b). Cicatrization becomes greatest in the adventitia and portions of the muscularis where the muscular fibers are destroyed. As healing progresses the inflammatory process recedes from the acute to the subacute, and finally to the chronic stage. The scar tissue contracts over a period of weeks and months

to produce as a general rule, a permanent structure of the ureter (Fig. 7). Healing is prolonged and epithelization is delayed.

Though the end of the ureter is first to be invaded its intramural extent and the adjacent parts of the intestine do not escape the inflammatory process. Infection spreads upward along the path of the ureter into the intermuscular planes and submucosa of the intestine. The mucosa itself shows minimal invasion probably because of a natural immunity to the fecal content. Sutures form rallying points for infection, and abscesses are prone to develop about them (Fig. 8). Areas of inflammation outside the ureter do not compress it. Except for constrictions and angulations caused by sutures which are placed improperly obstruction to the ureter is always produced by changes within its own wall.



Fig. The early traumatic manifestations seen in the intraluminal end of the ureter days following uretero-intestinal anastomosis. There are areas of hemorrhage best seen in the submucosa and diffuse edema with an infiltration of lymphocytes and plasma cells throughout all layers.

The end of the ureter sloughs more frequently in the presence of infection than from anemic necrosis alone. As cellulitis progresses, blood vessels and lymphatics become occluded, infectious gangrene results, and separation occurs at the point where sufficient vascularization ends. The greater part of this slough usually takes place soon after the first week, but it may be delayed for a month or more. Despite its own vulnerability to infection, the intestine gives the appearance of forming a protective covering around the submucosal course of the ureter, for, although it is common for a fulminating ureteritis to extend up to the place where the ureter enters the wall of the intestine, such a generalized infection rarely extends beyond it. The end often sloughs level with the rectal mucosa, but not proximal to this point, except in instances of massive necrosis, as will be described. A cross circulation from the intestine lends added vitality to the ureter soon after the first week.

The effects of these pathological changes

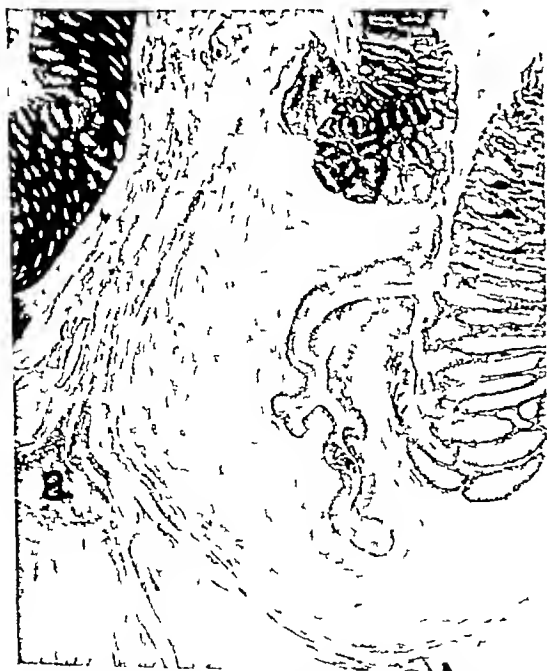


Fig 2 Ureterointestinal orifice following healing by primary union. Note the perfect fusion of the ureteral with the rectal mucosa and the coaptation of the two musculatures. a, Shows a foreign body reaction in the region of a suture.

upon the lumen of the ureter were observed following injection with gelatin. In localizing areas of obstruction, it is important not only to note a diminution in the normal caliber of the lumen but equally valuable to observe substantiating evidence from the effects of back-pressure on the kidney and ureter proximal to an area of suspected narrowing. Taking cognizance of both these features it was discovered that, in acute ureteritis, the lumen of the entire intraluminal segment is usually compressed. Later the very tip of the implanted ureter is the initial and most frequent site for the development of a stricture (Fig 9). If more scar tissue is formed, the area of constriction involves the remainder of the intraluminal portion (Fig 10). It is unusual for the process to advance into the intramural segment although this sometimes occurred after a period of several months (Fig 11).

The question naturally arises as to how obstruction in the end of the ureter may be avoided. We have shown that the reduction of infection in the field of implantation (1) is conducive to the prevention of ureteritis with its attendant stasis and later formation of stricture.

We attempted to evaluate, as another factor, the relative advantages of implanting a long or a short end of ureter at operation. In an experimental series of ureterointestinal anastomoses, an end less than 1 centimeter in length was utilized on one side, while the end



Fig 3 Anemic necrosis of the intraluminal segment of the ureter caused by the pressure of a catgut cylinder, 2 days following ureterointestinal anastomosis. The ureter is seen as only a ghost of its normal structure. The catgut cylinder lies within the lumen.

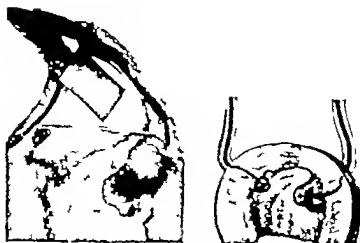


Fig 4 Ideal ureterovesical communication 5 weeks following bilateral ureterocystostomy. There is no constriction of either ureter. A small papilla remains on the right, long papilla on the left. The kidneys and ureters above are normal.

of the opposite ureter was left 3 centimeters long. Although an accurate statistical analysis of this factor was precluded by the complexity of other considerations, we concluded that the shortest possible end which is technically feasible is the most desirable. Since the intraluminal segment bears the brunt of the inflammatory reaction and is the area most consistently narrowed by acute inflammation as well as by the later formation of stricture, it seems rational to reduce its dimensions to an absolute minimum. Furthermore the exposed surfaces of the adventitia unpro-

ected by mucosa or by the wall of the intestine afford the best possible foothold for the entrance of infection.

We have found that our best results are obtained by dividing the end of the ureter tangentially and carrying a longitudinal incision a short distance beyond. Starting at the most proximal point of the beveled end, the wall is divided longitudinally almost to the level at which it is to emerge from the intestine. This step reduces the possibility of occlusion which, as we have demonstrated, is so likely to occur in a long, redundant end and brings the new orifice close to the protected intramural portion of the ureter. Furthermore it opens a broad expanse of ureteral mucosa to promote fusion with that of the intestine.

In our experience the Coffey No. 3 Higgins method and other operations depending on a transfixion suture for the establishment of an orifice are complicated by a higher incidence of obstruction and ascending infection. There is a tendency for the minute orifice to contract from cicatrization and, in a few instances, complete occlusion has occurred. The temporary period of absolute ureteral obstruction is a serious disadvantage of the Coffey No. 3 procedure. One inherent danger of any method which incorporates a transfixion suture is the possibility that the suture may fail to slough through.



Fig 5 Ideal ureteroileostomal communication 6 weeks following right subcutaneous transplant. There is no constriction or dilatation of the ureter. The upper urinary tract is normal.

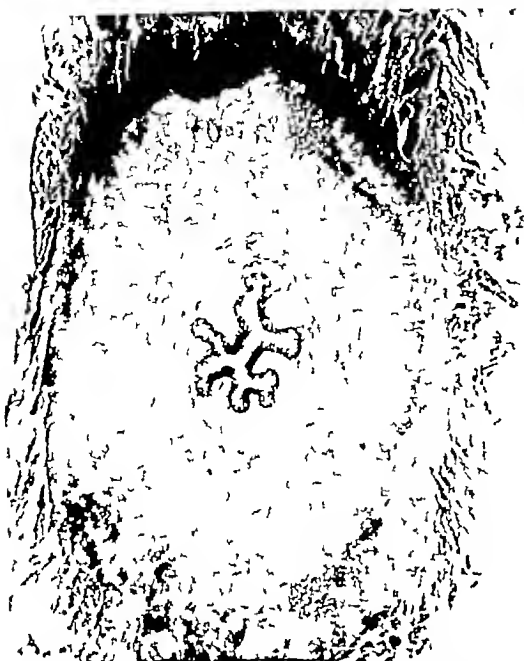
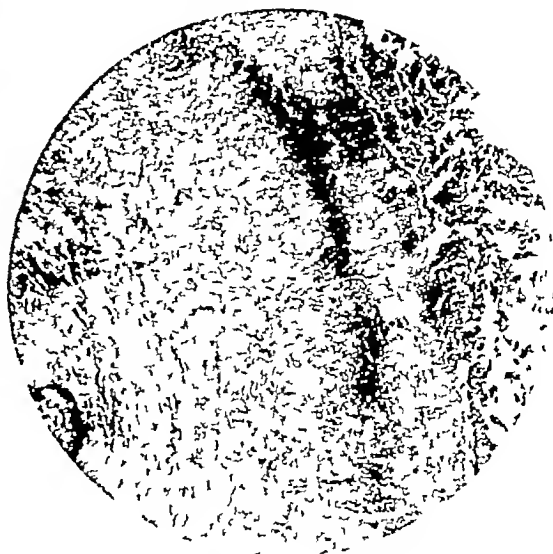


Fig 6 Acute inflammatory reaction involving the stump of the implanted ureter 1 week following ureterointestinal anastomosis. Leucocytes chiefly of the polymorphonuclear



strain are seen in all layers. The surface of the stump is encased in an inflammatory debris containing conglomerations of bacteria, best seen as dark areas in the high power photomicrograph, right. This view likewise shows the formation of granulation tissue, evidenced as fibroblasts and new capillaries in a zone surrounding the muscularis. Note the formation of cysts in the mucosa as a result of inflammation.

Transplantation of the ureter is possible only because the blood supply derived from the upper and middle portions is adequate to

nourish its entire length. Since some vessels course through the adventitia, care must be

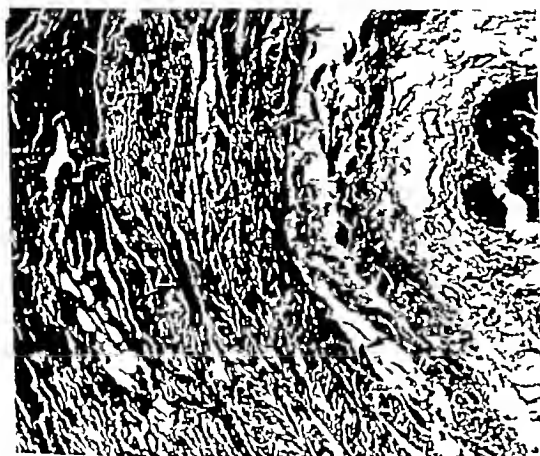


Fig 7 Stricture of the intraluminal segment of the ureter 6 weeks following submucosal ureterointestinal implantation. The arrows indicate the marked atrophy and replacement of the muscularis by scar tissue as demonstrated by connective tissue stain. (The gross specimen is illustrated in Fig 10.)

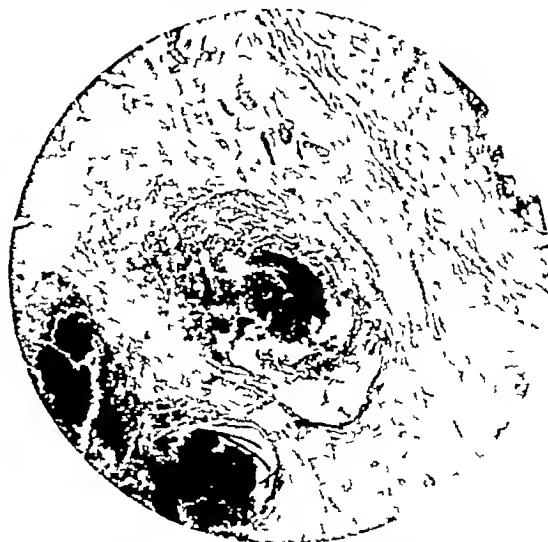


Fig 8 Acute ureteritis in the intramural segment of the ureter 18 days following ureterointestinal anastomosis. Note how silk sutures form rallying points for the formation of abscesses.

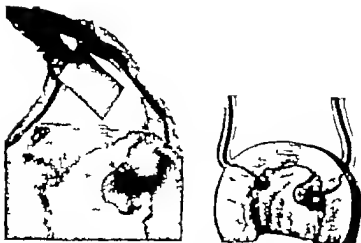


Fig. 4. Ideal ureterovesical communication 5 weeks following bilateral ureterocystostomy. There is no constriction of either ureter. A small papilla remains on the right, long papilla on the left. The kidneys and ureters above are normal.

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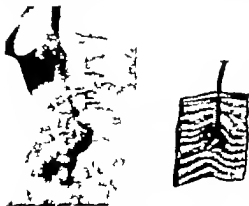


Fig. 5. Ideal ureterointestinal communication 6 weeks following right subhepatic transplant. There is no constriction or dilatation of the ureter. The upper urinary tract is normal.



Fig 12 Infectious gangrene involving the intramural segment of the ureter 3 days after a right submucosal implantation with the use of a catgut cylinder

had been implanted into the rectum came into contact and, incident to the infectious process, became fused into an inseparable mass. A similar fusion giving rise to more disastrous consequences, was occasionally noted within the lumen of the ureter, sealing it shut at the place where it had been crushed by a ligature

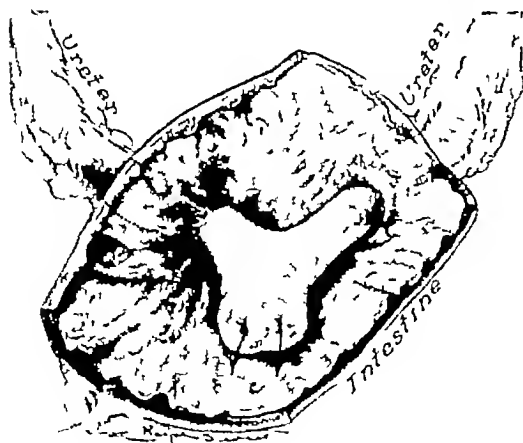


Fig 14 Ureteritis adhesiva. Two long ends of ureter which were implanted into the rectum came into contact and incident to the infectious process, became fused into an inseparable mass. The specimen is from a dog killed 2 months after a bilateral submucosal ureterointestinal anastomosis

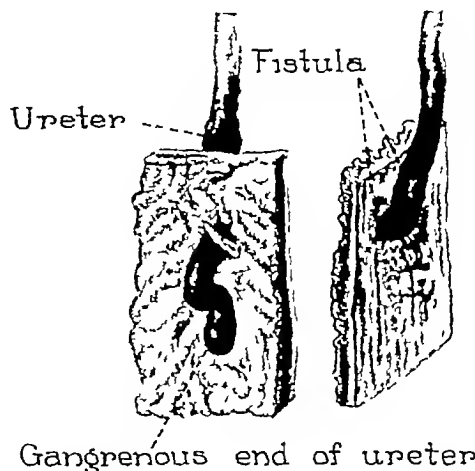


Fig 13 Infectious gangrene of implanted ureter extending 2 centimeters above the site of anastomosis. The dog succumbed, 5 days after a right ureterointestinal implantation, to peritonitis caused by leakage around the ureter and a fistula in the ureter itself

in our first application of the divisible carrier (Fig 15). In most instances the lumen became re-established, but in a few it remained permanently occluded. In still others an orifice at the side was formed at some point proximal to the tip. To prevent these complications, as mentioned previously, we now divide the end of the ureter tangentially, slit it longitudinally for a short distance beyond, and affix the divisible carrier to its very tip. Urinary contamination is prevented during this stage

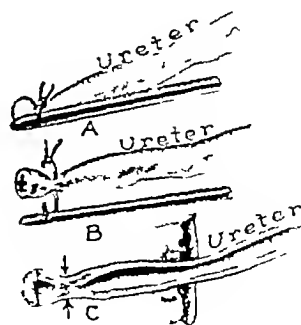


Fig 15 Diagram illustrating how crushing the end of the ureter by a ligature during operation may lead to an adhesive process within the lumen and give rise to partial obstruction, or even to occlusion



Fig. 9a.

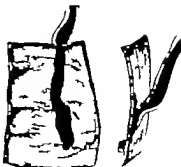


Fig. 9b.



Fig. 10a.



Fig. 10b.

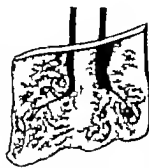


Fig.

Fig. 9. Marked constriction at the ureterointestinal orifice which opens on small papilla. The intraluminal and intramural portions are widely dilated and marked hydro-ureter and hydrophrosis are present. The specimen is from dog killed 1 month following left submucosal ureterointestinal anastomosis.

Fig. 10. Constriction of the intraluminal segment of the ureter causing its dilatation of the intramural portion and

marked hydro-ureter and hydrophrosis above. The specimen is from dog killed 6 weeks after right submucosal ureterointestinal anastomosis.

Fig. 11. Constriction of the intraluminal and intramural portions of the ureter giving rise to bilateral infected hydro-ureter and hydrophrosis above. The specimen is from dog killed 4 months after bilateral submucosal ureterointestinal anastomosis.

taken not to denude the ureter too completely preparatory to an anastomosis. Occasionally the blood supply is so completely destroyed that an anemic necrosis of the ureter reaches above the site of implantation. When this occurs leakage is inevitable and peritonitis ensues. Infectious gangrene giving rise to a massive necrosis may produce the same result. The danger of this complication is likewise increased by injury to the blood supply (Figs. 12 and 13).

In some of the operations the peritoneum covering the lower portion of the ureter was dissected with the ureter and used as a cuff

around it in implanting the end into the bowel. This has been recommended as a measure to assure the preservation of an adequate blood supply. At necropsy however we noted no decrease in the incidence of infection and obstruction in the ends of the ureters so treated. Ureteritis and sloughing of the ends occurred as usual with the peritoneum participating in the process.

A pathological characteristic which sometimes plays a part in shaping the final result is the adhesive quality of inflamed surfaces. This is displayed by the specimen illustrated in Figure 14. Two long ends of ureter which



Fig 12 Infectious gangrene involving the intramural segment of the ureter 3 days after a right submucosal implantation with the use of a catgut cylinder

had been implanted into the rectum came into contact and, incident to the infectious process, became fused into an inseparable mass. A similar fusion giving rise to more disastrous consequences, was occasionally noted within the lumen of the ureter, sealing it shut at the place where it had been crushed by a ligature

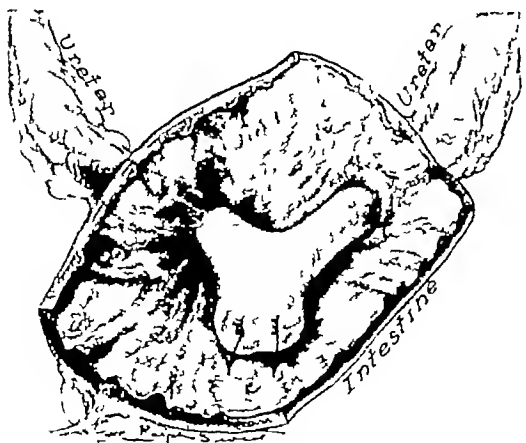


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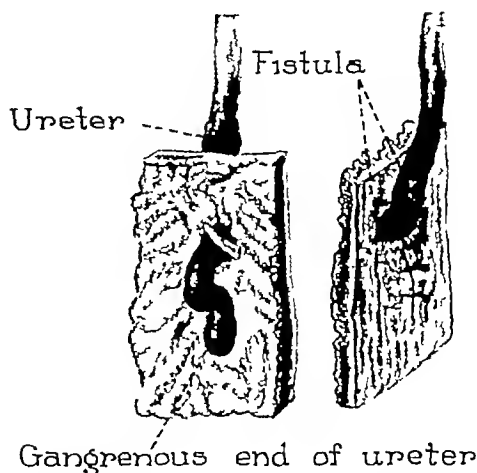


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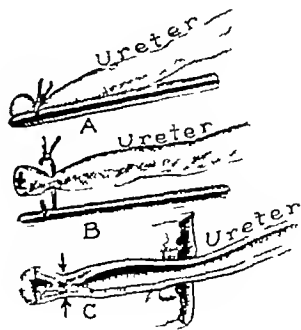


Fig 15 Diagram illustrating how crushing the end of the ureter by a ligature during operation may lead to an adhesive process within the lumen and give rise to partial obstruction, or even to occlusion

of the operation by temporary occlusion of the ureter with a bull-dog clamp. Gentle handling is important in order to minimize trauma with its resultant necrosis and infection.

We have demonstrated that ureteral obstruction and ascending infection following uretero-intestinal anastomosis are attributable to the highly contaminated nature of the contents of the large intestine (1). In this paper we have traced the pathological changes which occur in the implanted ureter and have shown that the end of the implanted ureter is a region of crucial importance as concerns a successful result. Subsequent communications will be devoted first, to the effect of these changes upon the upper urinary tract, especially to the relationship between ascending infection and ureteral obstruction (2) and, secondly to the methods of reducing the infectious changes of the implanted portion so that primary healing of the end of the ureter will occur (3).

SUMMARY

The end of the implanted ureter constitutes an area of crucial importance in determining

the success or failure of a uretero-intestinal anastomosis. The pathological changes which occur in this structure are carefully traced, especially with a view to demonstrating the hazards which accompany damage to the blood supply and the entrance of infection if extending above the site of the anastomosis, either anemic necrosis or infectious gangrene gives rise to fatal peritonitis. A virulent infection in the ureteral stump causes serious damage to the upper urinary tract first by acute ureteritis with its attendant stasis and later by the formation of stricture. The changes in the end of the ureter therefore play a great part in accounting for the morbidity and mortality both early and late which attend the operation.

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EXCISION OF THE HEAD OF THE PANCREAS FOR CARCINOMA WITH STUDIES OF ITS BLOOD SUPPLY

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DURING the past 15 years many advances have been made in the surgical treatment of carcinoma of the ampullary region of the duodenum. By far the greatest number of cases of obstructive jaundice due to this cause have been treated by a palliative type of operation in which the gall bladder or common duct has been anastomosed to the stomach or duodenum. It is remarkable that so few attempts at excision of carcinoma localized to this region have been attempted when one realizes that the first operation of this type was done as long ago as 1900 by Halsted. Up to 1927 Cohen and Colp were able to collect only 59 cases in which local excision of carcinoma of the ampulla was accomplished and, though only a relatively small number of these patients survived the operation more than a few days, there were 4 patients who lived beyond 18 months. This report apparently stimulated many surgeons to do the local excision type of operation, so that by 1935 Whipple, Parsons, and Mullins (16) were able to add 20 reported cases to those collected by Cohen and Colp, and in the same year Hunt and Budd found in the literature a total of 76 cases which had been treated in this manner.

Up to this time the lesion had been excised locally with, in the majority of cases, reimplantation of the bile duct, and in 1932 Walters first suggested that the immediate mortality rate from the operation could be reduced if it were preceded by a cholecystostomy. Whipple, Parsons, and Mullins, in their report in 1935, suggested a wide excision of the adjacent pancreas and duodenum for the first time, thus sacrificing the external secretion of this gland and substituting a gastroenterostomy in place of any attempt to preserve the duodenum. This proposed change was based on the following facts: (1) For many years it had been

realized that the external secretion of the pancreas was not essential to life in animals, and it was thought that one could sacrifice it in man without ill effects. (2) A great many postoperative deaths from local excision of the ampulla were due to leakage of pancreatic secretion around the anastomosis which, of necessity, was formed between the amputated ends of the ducts and the duodenum. (3) Whipple stressed that the operation of wide excision, sacrificing the external secretion of the pancreas, conformed to the main principle of cancer surgery in excising large blocks of tissue wide of the growth. This last consideration is of extreme importance, for many cases will show extension into the wall of the common duct itself or the adjacent pancreas, and there is really no point in attempting to excise these lesions if one does not seriously attempt to remove all cancer tissue.

Since this more radical excision is much more time-consuming and involves more risk of shock to the patient who is already in a precarious position as a result of long-standing complete obstruction of the lower end of the bile duct, and in many cases of the pancreatic ducts, Whipple suggested that the operation be done in two stages. The first stage involved a cholecystgastrostomy and gastroenterostomy followed 4 to 6 weeks later by a wide excision of the lesion, a major portion of the duodenum being sacrificed and the previous gastroenterostomy relied on for re-establishment of the continuity of the gastrointestinal tract (Fig. 1).

Following this momentous contribution to the surgery of this region, numerous reports have appeared in the literature attesting to its sound principles and success. In 1938 Whipple (15) again made an important suggestion when he advocated a further change in the technique of the first stage because the cholecystgastrostomy had been found to possess certain defects. The fundamental principle of

of the operation by temporary occlusion of the ureter with a bull-dog clamp. Gentle handling is important in order to minimize trauma with its resultant necrosis and infection.

We have demonstrated that ureteral obstruction and ascending infection following ureterointestinal anastomosis are attributable to the highly contaminated nature of the contents of the large intestine (1). In this paper we have traced the pathological changes which occur in the implanted ureter and have shown that the end of the implanted ureter is a region of crucial importance as concerns a successful result. Subsequent communications will be devoted first, to the effect of these changes upon the upper urinary tract especially to the relationship between ascending infection and ureteral obstruction (2) and, secondly, to the methods of reducing the infectious changes of the implanted portion so that primary healing of the end of the ureter will occur (3).

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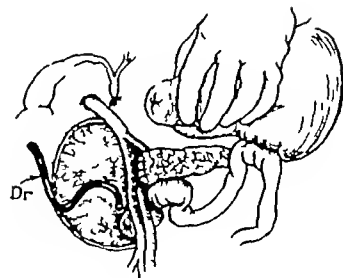
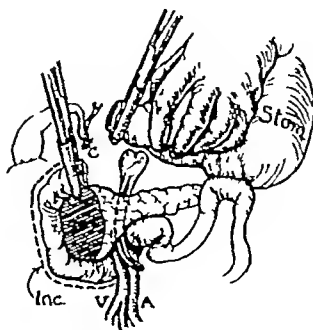
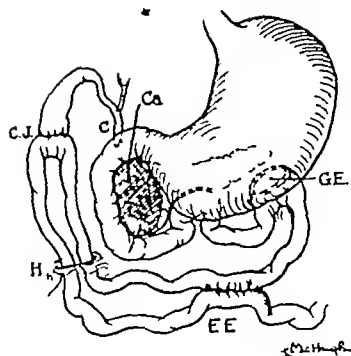
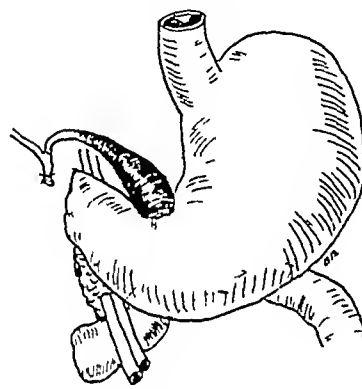
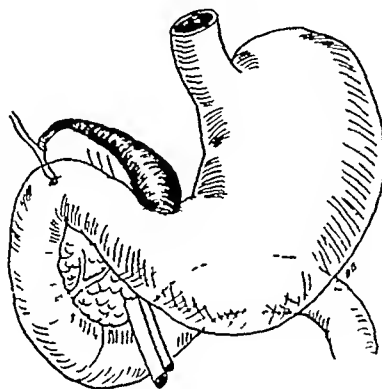


Fig 3, above. The Brunschwig method. The entire head of the pancreas was resected for carcinoma (*Surg, Gynec & Obst*, 1937, 65 681)

Fig 4, right. The method of George Crile, Jr, used to excise the head of the pancreas for carcinoma (Courtesy, *Am J Surg*, 1940, 47 91)



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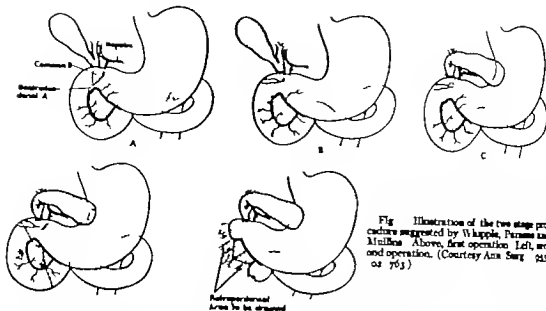


Fig. 1. Illustration of the two stage procedure suggested by Whipple, Parsons and Mullins. Above, first operation. Left, second operation. (Courtesy Ann Surg 915, 25, 765.)

radical excision *en bloc* of the tumor by means of a two stage procedure remained unchanged. However he was disturbed by numerous instances in which recurring cholangitis and hepatitis followed the first stage in spite of the provision of a large stoma between the gall bladder and the stomach. It was apparent by this time that the lack of pancreatic secretion

did not interfere with the patient's nutrition. In fact, most of the patients constantly showed a gain in weight following the first stage of the operation. He proposed, therefore, a cholecystojejunostomy on the Roux principle, as shown in the accompanying diagram (Fig. 2) and reported 3 cases, none of which had been followed by cholangitis.

One point which should be borne in mind is that the mesentery of that portion of the jejunum forming the anastomosis with the gall bladder should be sutured to the parietal peritoneum at a considerable distance from the duodenum in order that the division of the peritoneum along the lateral border of the duodenum, at the second operation can be accomplished without interfering with this leaf of mesentery. Furthermore, although Whipple recommends the ligation of the common duct just below the entrance of the cystic duct at the first operation. It is suggested that the common duct be left undisturbed so that one will not be hampered at the second operation by the presence of many adhesions in this region. If however the common duct has been opened for exploration during the first stage of the operation, it probably is wise to ligate it and leave a long silk suture for a marker as he suggests.

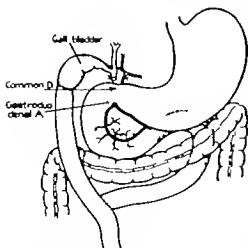


Fig. 2. Illustration of the change in the first stage operation to that of cholecystojejunostomy on the Roux principle as suggested by Whipple. (Courtesy Am J Surg 935, 40, 26.)

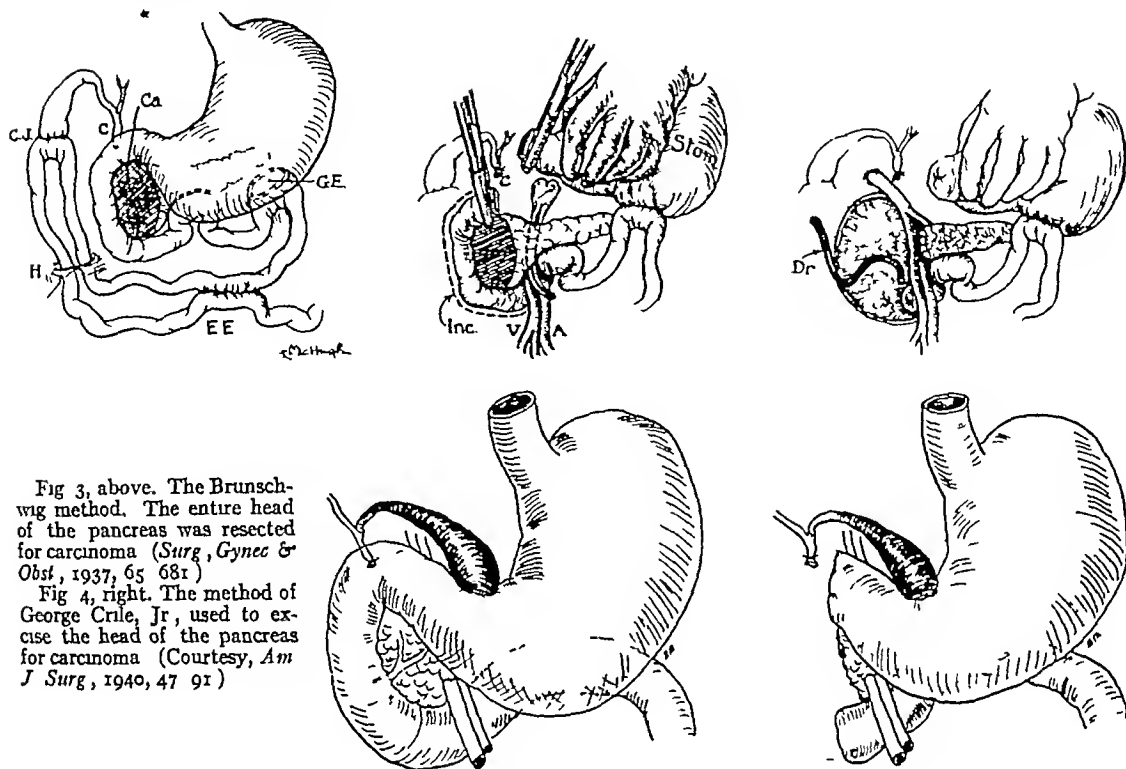


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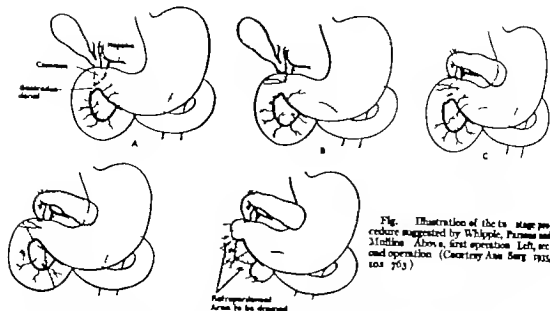


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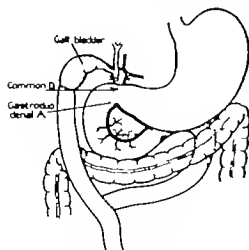


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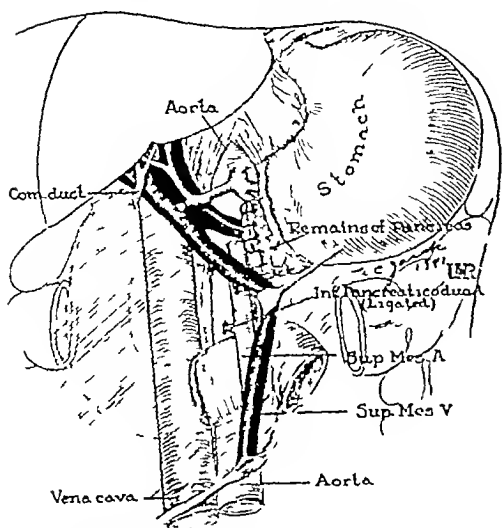


Fig 7 The completed operation with gastroenterostomy not shown

are used throughout. The pylorus is first divided and this immediately exposes the pancreas where a blunt instrument can be passed beneath the neck of the gland. Caution must be used to keep the instrument in close proximity to the deep surface of the gland for several important large vessels lie immediately behind it. The neck is then divided along the line shown in Fig 5b. We used the actual cautery for this division feeling that bleeding would thereby be better controlled and the danger of leakage of pancreatic secretion decreased. However, Tripodi and Sherwin, in recent experiments on excision of the pancreas in dogs, have shown that the stump of the pancreas heals equally well and shows no tendency toward leakage of its external secretion whether one uses the scalpel, actual cautery, or high frequency knife. It probably would be safer to make the division with the scalpel, since there is actually very little bleeding from this portion of the pancreas and one could then more easily identify and ligate the main pancreatic duct issuing from the body of the gland. The first part of the duodenum is then mobilized from above, no attempt being made to separate it from the pancreas, and in the course of this part of the dissection the gastroduodenal artery and common bile duct are ligated and divided.

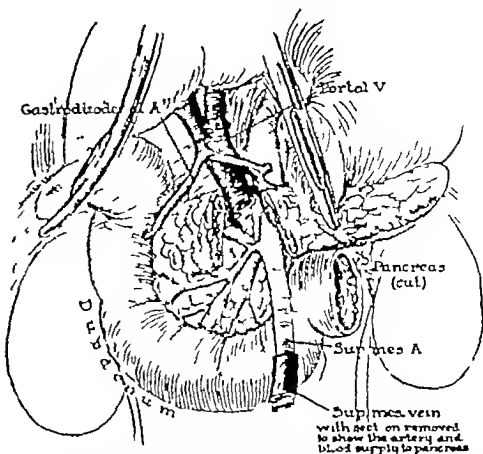


Fig 8 Portion of the superior mesenteric vein has been removed to show the high origin and fan shaped distribution of the inferior pancreaticoduodenal artery

By dividing the pancreas at this point one immediately exposes the splenic and superior mesenteric veins where they join to form the portal vein, and it will be seen that the latter crosses the head of the pancreas in an oblique fashion, the superior mesenteric artery lying behind and hidden by the vein (Fig 6a). Numerous small veins issuing from the head of the pancreas enter the superior mesenteric vein on its pancreatic surface, and these must be ligated while the vein is gently retracted medially in order to expose the upper and medial margins of the head as shown in Figure 6b. From this point on in the operation we

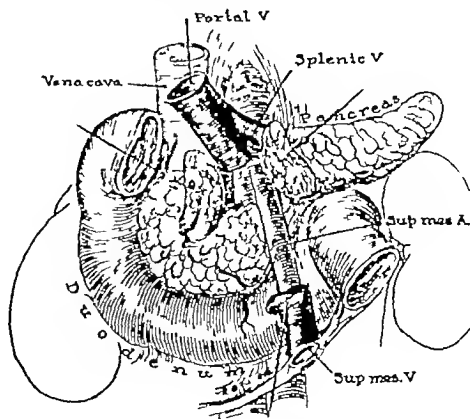


Fig 9 Depicting the usual origin, course, and distribution of the inferior pancreaticoduodenal artery described in most textbooks of surgery and anatomy

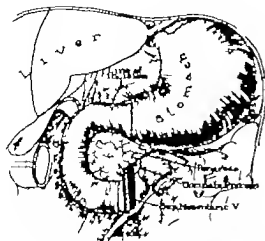
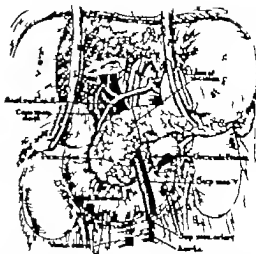


Fig. 5. a, left. The area of duodenum and pancreas to be excised outlined by the dotted line. b, Exposure after



the division of the pylorus. The dotted line indicates the line of incision through the neck of the pancreas.

OPERATIVE PROCEDURE

Last year I attempted an operation for excision of carcinoma of the head of the pancreas which presented several interesting problems. The first stage of this operation required a choledochojejunostomy due to the fact that the patient possessed a nonpatent cystic duct and a small, scarred gall bladder which could not be utilized in a short-circuiting operation.

Unfortunately this contributed to the patient's death following the second stage due to a separation of the suture lines as a result of traction on this region and consequent leakage of bile.

The second stage of the operation, as described by Brunschwig, is illustrated by Figures 5, 6 and 7. A transverse incision is employed to open the abdomen and silk sutures

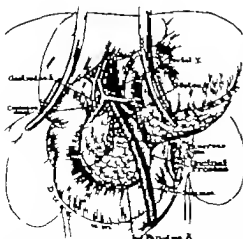


Fig. 6. a, left. Exposure of the superior mesenteric vessels by division of the neck of the pancreas and the projection of the uncinate process behind and medial to these vessels. b, Retraction of the head of the pancreas laterally and the mesenteric veta medially the uncinate process



of the head thus being freed. Several pancreatic veins have been ligated, as have the gastroduodenal artery and the common bile duct. The so-called normal origin of the inferior pancreaticoduodenal artery is shown in this drawing.

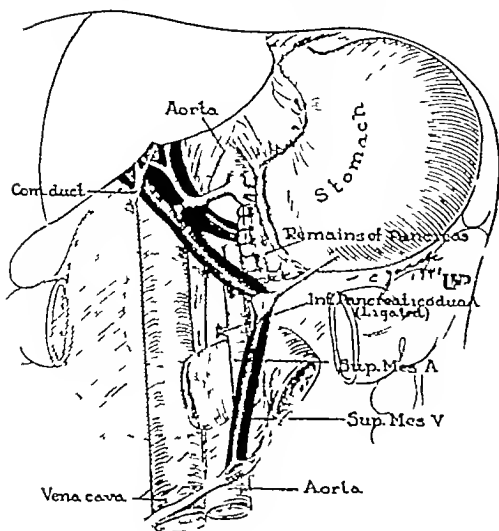


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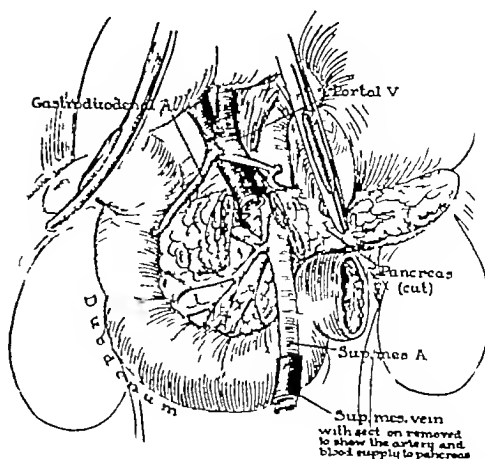


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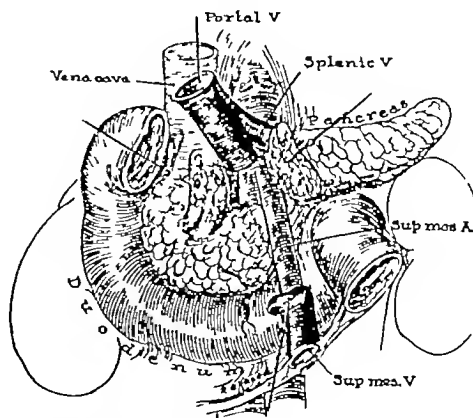


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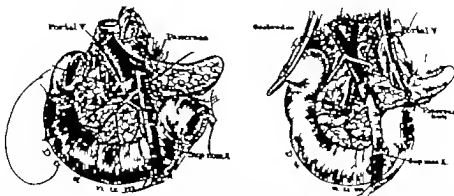


Fig. 6. a, left and b. T. side of the 24 dissections studied revealed high origin of the inferior pancreaticoduodenal artery as shown. (A section of the superior mesenteric vein as removed to clarify the picture)

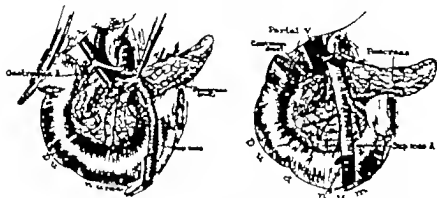


Fig. 7. a, left and b. A high posterior origin of the inferior pancreaticoduodenal artery

encountered several interesting and unexpected difficulties. The duodenum has been mobilized by division of the lateral reflexion of peritoneum and by blunt dissection the hand can be placed behind the duodenum and head of the pancreas where these structures lie immediately adjacent to the vena cava and aorta. In order to carry the dissection around the medial border of the head it is necessary to provide some traction to free the uncinate process from its position beneath the superior mesenteric artery. When this maneuver was attempted in our patient he immediately developed a profound state of shock which persisted until the close of the operation and for 2 to 3 hours afterward in spite of all the usual methods which were used to combat it. We believe that this was due to the fact that the head of the pancreas is abundantly supplied

with sympathetic nerves issuing in a radiating fashion from the plexus around the root of the superior mesenteric artery. In a good many cases this traction can be avoided but it is suggested that in order to prevent this sympathetic reflex from operating, one should inject the region of the plexus with novocain as soon as the neck of the pancreas has been divided.

The next problem which we encountered was that the inferior pancreaticoduodenal artery does not always arise low on the superior mesenteric artery and proceed laterally in the interval between the pancreas and duodenum as described in most textbooks of surgery and anatomy. In the case under discussion it had its origin high up near the root of the artery and proceeded downward and outward, as shown in Figure 8. This caused us some concern inasmuch as we were doubtful whether or

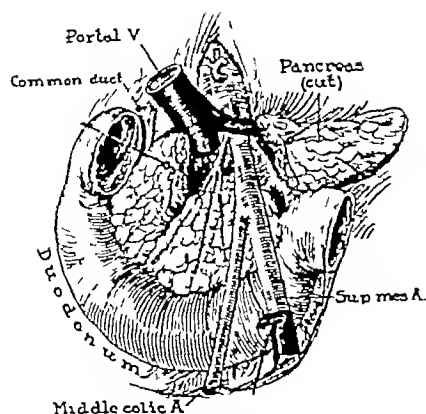


Fig 12 Another case of high origin of the inferior pancreaticoduodenal artery and the only case in which its branches reached the pancreas and duodenum on its posterior aspect

not this vessel could be ligated at its origin without endangering the vitality of the third portion of the duodenum at that point where we intended to amputate it and turn in the distal end. We felt that primary ligation of this vessel and the gastroduodenal artery as early as possible in the operation would render the resection relatively bloodless and conserve much time otherwise occupied in the ligation of numerous small bleeding points. The operation should be completed by inverting the stump of remaining duodenum, closing the stump of the body of the pancreas with three or four silk mattress sutures and the provision of a posterior gastroenterostomy as shown in Figure 7. Our patient, however, was in such a severe stage of shock that we saved some time by sewing the stump of the duodenum to the distal end of the stomach. In the future it would be better to do the gastroenterostomy as the first step in the second stage rather than be faced with this at the close of the operation. Shock, if it develops at all, is most likely to occur when one uses traction on the head of the pancreas, and one should be in a position to close the abdomen at once. In our case this was accomplished with through-and-through wire sutures without drainage. The patient died 3 days later of bile peritonitis due to a leakage from the previous choledochojejunostomy and a complete thrombosis of the portal vein and its tributaries. I cannot ex-

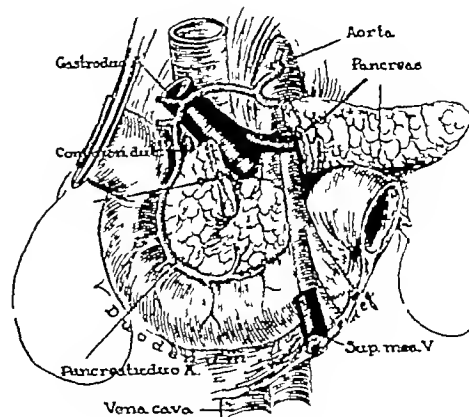


Fig 13 The only case in the group in which no inferior pancreaticoduodenal artery was present.

plain the development of the portal thrombosis and it is regrettable that it occurred, for there was a concomitant gangrene of the stomach and jejunum so that we were unable to determine whether or not the ligation of the inferior pancreaticoduodenal artery interfered with the vitality of the duodenal stump.

STUDIES OF THE BLOOD SUPPLY OF THE HEAD OF THE PANCREAS AND DUODENUM

The finding of the high origin of the inferior pancreaticoduodenal artery led to an anatomical investigation of the blood supply of the head of the pancreas with particular reference to this artery. With the co-operation of Dr W B Hawkins in the department of pathology and Prof Karl Mason in the department of anatomy, 24 dissections were carried out, in each instance the operative approach described above being used, examples of these are illustrated by Figures 9 to 16. In only 8 of the subjects were we able to demonstrate the normal textbook picture of the artery as depicted in Figure 9. In 12 instances, comprising half of the subjects studied, the artery arose from a high position on the superior mesenteric, frequently from its posterior aspect (Figs 10a, b and 11a, b). The artery immediately breaks up into many smaller vessels which proceed in a fan-shaped distribution to the anterior surface of the pancreas and third portion of the duodenum. Figure 12 reveals a very high origin of the artery and is the only instance in which its branches reached the

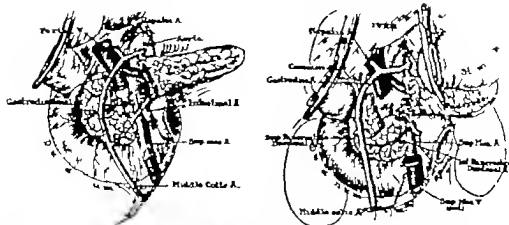


Fig. 14. a, left, and b. The abnormal origin of the middle colic artery from the gastroduodenal artery

head on the posterior surface. This subject also presented a very high origin of the middle colic artery which then pursued a course across the duodenum at the point where it would be turned in during the operation. Further dissection of this group of high origins of the inferior pancreaticoduodenal artery revealed that, as a general rule the first intestinal branch arose from the posterior surface of the superior mesenteric artery above the duodenum and supplied the terminal portion. In these cases therefore, there probably exists an adequate blood supply to that portion of the duodenum which would be transected and turned in during the operation in spite of the high ligation

of the inferior pancreaticoduodenal artery at its point of origin.

One dissection revealed no vessel corresponding to the inferior pancreaticoduodenal (Fig. 13). The 3 subjects, illustrated by Figs. 14a, b and 15 show a most unusual and unsuspected anomaly. In 2 of these the middle colic artery has arisen as a main branch from the gastroduodenal. In such a case, it can be readily seen that ligation of the gastroduodenal artery early in the operation as suggested, before discovery of this anomaly might result in a serious impairment of the arterial supply of the transverse colon. With the exception of this anomaly the early ligation of the gastro-

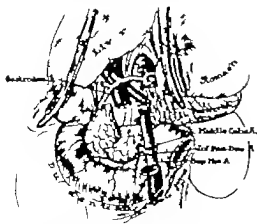


Fig. 15. In this case the inferior pancreaticoduodenal artery arose from the middle colic artery

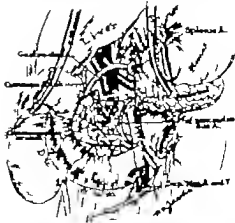


Fig. 16. Normal origin of inferior pancreaticoduodenal artery. Many anastomotic vessels supply the pancreas.

duodenal artery at its origin is possible in the operative technique described, for it was remarkably constant in its origin, course, and distribution in all 24 dissections. In the other case (Fig 15) the inferior pancreaticoduodenal artery is a branch from the middle colic, and here again an unfortunate arterial ligation would be possible. Figure 16 demonstrates a very peculiar arrangement of aberrant vessels forming a perplexing anastomosis on the anterior surface of the pancreas.

SUMMARY

1 A case is presented in which a two stage resection of the entire head of the pancreas for carcinoma was accomplished, and it is recommended that the first stage be that of a cholecystjejunostomy following the Roux principle as advocated by Whipple.

2 The actual excision of the entire head of the pancreas, rather than a partial wedge excision, together with the major portion of the duodenum, is feasible and can be greatly facilitated by ligating the gastroduodenal artery and the inferior pancreaticoduodenal artery early in the operation, thus the greater portion of the dissection is rendered relatively bloodless.

3 However, as a result of 24 dissections in which the various stages of the operation were carried out according to plan, certain marked deviations from the normal distribution of these vessels, as described in most textbooks of anatomy, have been exposed and might render this stage of the operation technically difficult.

4 These dissections disclosed that in half of the subjects studied the inferior pancreaticoduodenal arises high up on the superior mesenteric artery and is distributed in a fan-shaped manner downward and outward over the anterior surface of the gland.

5 The gastroduodenal artery is remarkably constant in its origin, course, and distribution,

but in 2 of the subjects studied it gave origin to the middle colic artery. It is, therefore, recommended that the origin and distribution of this vessel be determined before the gastroduodenal artery or the inferior pancreaticoduodenal artery are ligated.

6 In many cases traction laterally on the head of the pancreas is necessary in order to dislodge the uncinate process from its position beneath the superior mesenteric vessels. This maneuver may induce a reflex resulting in profound shock because of the large number of sympathetic nerves radiating to the pancreas from the mesenteric plexus. Therefore it is suggested that, as soon as the head of the pancreas is exposed, the plexus be infiltrated with novocain, in the hope that this complication, which we found extremely difficult to combat successfully, may be avoided.

7 The suggestion is made that the placing of a gastroenterostomy be the first step in the second stage of the operation.

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AN ASEPTIC RESECTION OF THE STOMACH FOR CARCINOMA AND ULCER

EMILE HOLMAN M.D. F.A.C.S., San Francisco, California

CARCINOMA of the stomach is frequently accompanied in patients of advanced age by anemia, debility, poor nutrition and impaired resistance to infection. Every effort is made before operation upon such patients to minimize the hazards imposed by these conditions by transfusions, by a high protein, high carbohydrate diet, and by the administration of vitamin concentrates for 7 to 10 days preceding the operation. Occasionally sulfanillamide and, more recently, sulfathiazole have been administered for 24 hours before the operation and for 48 hours after the operation. Despite these various precautions, which may not all be realized because of pyloric obstruction the hazards remain great. In one clinic, a mortality of 50 per cent has been recorded following resections. In the past 10 years at the Stanford clinic, the mortality in the resected cases has been 10 per cent. In an effort to reduce this mortality still further an aseptic resection of the stomach has been developed in the past 18 months, independently of a similar development in Wangenstein's clinic (6). Although primarily intended for applica-

tion in resection for carcinoma, in which, due to achlorhydria, infection is more imminent, we are now employing it also in resection for ulcer. In resection for ulcer it is freely conceded that in the majority of cases the contamination encountered by entering the lumen of the stomach, the duodenum, or the jejunum does not usually impose a serious risk of infection. However, since one or two patients in every hundred cases of resection of the stomach suffer infected wounds, and occasionally peritonitis and death, an aseptic technique should diminish or prevent such catastrophes. By such improvements and by constant vigilance and endeavor does the surgeon reduce "the irreducible minimum."

The accompanying illustrations show the various steps in technique.

In all upper abdominal surgery the optimum position of the patient on the table is obtained by elevation of the upper half of the body permitting the stomach and liver to descend below the costal margin, and the small intestines to fall into the pelvis out of the operative wound (Fig. 1a). This prevents exposure and handling of the small bowel, both important factors in postoperative distention. In this position also pulmonary

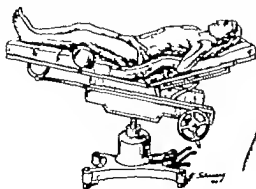


Fig. 1a.

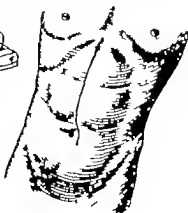


Fig. 1b.

From the Stanford University Medical School.
Presented before the Pacific Coast Surgical Association February 20, 1945.

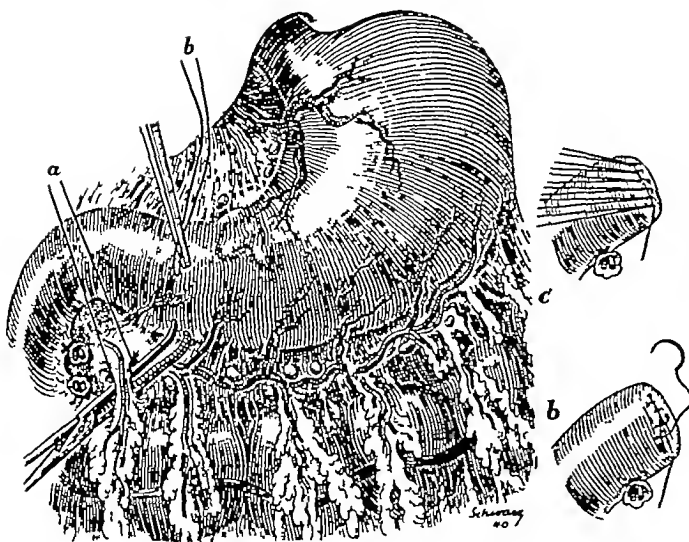


Fig 2a

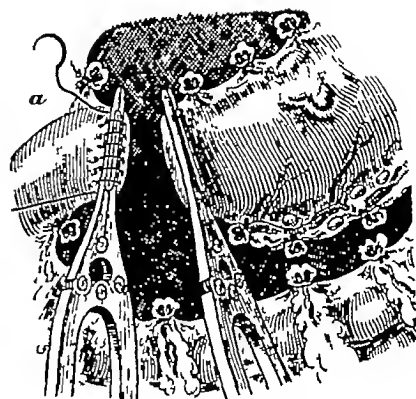


Fig 2b

ventilation and respiratory exchange is improved through a more efficiently working diaphragm. A kidney elevator maintains the normal lordosis and elevates the intra-abdominal contents into the wound. By flexion at the hips, the lower half of the body is elevated above cardiac level to prevent pooling of blood in the lower extremities incident to the general vasodilatation that accompanies a general anesthetic.

A midline incision (Fig 1b) provides easy accessibility both to duodenum and to the cardia of the stomach. On occasion the left costal cartilages close to the sternum are divided without entering the chest, and the ligamentous attachment of the left lobe of the liver is divided to expose the esophageal gastric junction. The incision may be prolonged on either side of the umbilicus as circumstances dictate.

In mobilizing the omentum or the gastrohepatic mesentery, the tissues containing the blood vessels are not crushed by the application of clamps (Fig 2a). Instead, the tissues are separated by blunt dissection in an avascular area, two ligatures are applied and tied, and the tissue cut between them. Where the tissue cannot be separated easily as in the gastrohepatic mesentery, the two ligatures are applied by transfixion needles introduced through an avascular area, and the vessel is divided be-

tween them. The purpose of avoiding clamps is to minimize the crushing and devitalization of tissues in the operative area—thus (1) reducing the postoperative febrile reaction, (2) eliminating as far as possible the need of the body to absorb dead tissue, and (3) minimizing still further the hazard of infection through possible bacterial contamination of avascular tissue capable of acting as an excellent culture medium. It is believed that if the cells in the avascular tissue beyond the ligature are not crushed, their nutrition may be maintained by becoming adherent to surrounding structures or by imbibition of nutrition from peritoneal fluid until revascularization is effected.

The stomach is mobilized, the lesser curvature almost completely, the greater curvature well up to and sometimes including the gastrosplenic ligament (Fig 2b). Two Payr clamps are applied distal to the pylorus and the duodenum is transected between them with a cautery. The distal duodenal stump is sealed by applying the cautery along the Payr clamp for approximately 15 seconds to insure coagulation of the vessels in the divided duodenal wall. A continuous Parker-Kerr basting stitch of No. 0 chromic catgut on an atraumatic needle is applied to the duodenum with the Payr clamp still in place (Fig 2b, a), thus insuring the turning in of the raw edges on



Fig. 5a.

Fig. 5b.

removal of the clamp. This first line of closure is in turn buried by reversing the direction of the same catgut suture back to its site of origin (Fig. 5b). A third line of interrupted black silk sutures is applied (Fig. 5b c) thus burying the two previously placed continuous catgut closures.

In line with previous observations (5) continuous nonabsorbable sutures are never used in gastrointestinal anastomoses. Reichert and Holman found in cleared specimens of intestinal anastomoses of 3 to 6 weeks duration that the interrupted nonabsorbable silk sutures had migrated so that they lay either underneath the peritoneum, or had been discharged into the lumen and lost. The determining factor seemed to be whether or not the suture had passed into the infected mucosa. If the needle was made purposely to penetrate the lumen, the stitch was discharged into the lumen. If the needle was applied to pass through the submucosa without entering the lumen, the stitch would eventually lie free on the serosal surface covered only by peritoneum. Therefore a continuous nonabsorbable

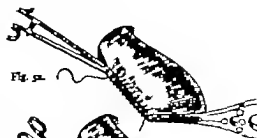


Fig. 5c.



Fig. 5d.

stitch might lie partly underneath the peritoneum, and partly inside the lumen, thus providing a continuous "seal" from sterile peritoneum to the infected lumen. Hence, the necessity of avoiding the use of continuous nonabsorbable sutures in intestinal anastomoses.

The Parker Kerr *inversion* stitch is a fundamental procedure in surgery. It turns into the intestinal lumen the raw contaminated edge of the divided bowel wall and approximates serosa to serosa (Fig. 3b). As early as 1823 Bichat enunciated this elemental fact, to be applied by Lambert in 1826 to intestinal suturing. Despite the insistence of these early authors that mucosa-to-mucosa will not heal, that serosa-to-serosa is a *sine qua non* in inter-

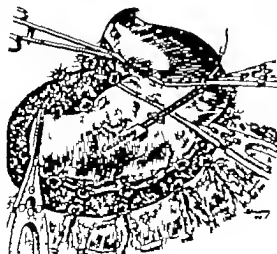


Fig. 6a.



Fig. 6b.

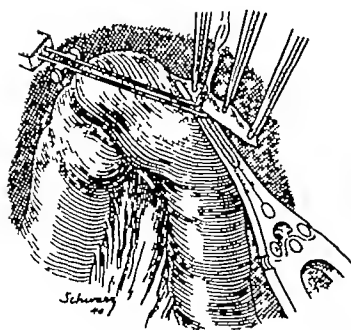


Fig 6a

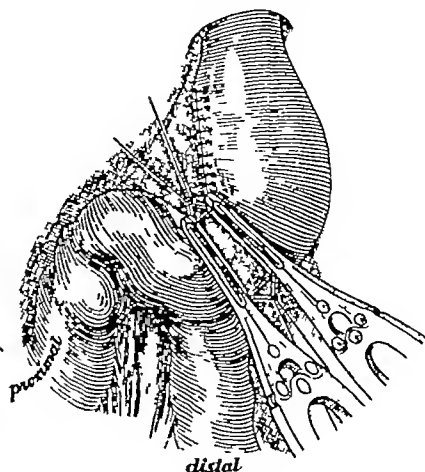


Fig 6b

tinal suture, some surgeons are still fond of using either the mattress *eversion* stitch for approximation of surfaces and control of bleeding, or the de Petz clamp, which everts the unsterile bowel edges and applies constricting metal staples to control bleeding (Fig 3a). The raw edges approximated by this mucosa-to-mucosa stitch are then buried by a serosa-to-serosa suture, thus fulfilling the law of intestinal suturing. However, the buried raw edges of the bowel, infected and avascular, theoretically may invite the formation of small abscesses which may burst into the lumen or the peritoneal cavity, and may cause failure in the line of suture with the formation either of an external fistula or a peritonitis. Granting that this may occur only rarely, its very possibility should be eliminated by avoiding the *eversion* stitch in intestinal suturing.

Payr or narrow crushing clamps are applied to the stomach in one of two ways (Fig 4a and b), as illustrated, depending upon the ease of application. The stomach is divided with a cautery, and the cut edges of the stomach wall are seared by passing the hot cautery back and forth over the surface of the clamp for 15 seconds. Recently, following the observations of Gerbode in the Stanford Surgical Laboratory, instead of the stomach being divided flush with the crushing clamp, a small cuff of the wall is left projecting 1 to 2 millimeters beyond the clamp. This cuff is seared, thus coagulating and closing the open ends of blood

vessels without damaging the gastric wall on the proximal side of the clamp, which may occur if the clamp is excessively heated. Gerbode's observations indicate that the portion of the bowel wall devitalized by the crushing clamp and by the cauterization separates and drops off into the lumen within 48 hours. The resulting raw surface between the opposed intestinal walls which is usually very narrow is covered with mucosa within 18 to 21 days.

The remnant of stomach is partially closed along the lesser curvature, first by a continuous Parker-Kerr basting stitch of chromic catgut on an atraumatic needle (Fig 5a), thus inverting the raw seared surfaces of the divided stomach wall. The continuous suture is in turn buried by interrupted silk sutures (Fig 5b). A Payr or narrow-bladed Martzloff or Wangenstein clamp is applied tangentially on the jejunal wall as illustrated in Figure 6a and a segment is removed by cautery, the edges of the bowel being seared again for about 15 seconds to control bleeding. Careful inspection of the removed segment should reveal a mucosal surface along its entire extent.

The loop of jejunum is applied to the stomach remnant (Fig 6b), proximal arm to right of opening, distal arm to greater curvature.

The two Payr or Wangenstein narrow-bladed clamps on the remnant of stomach and on the jejunum are approximated anterior to the colon (Fig 7). The anastomosis is effected by one of two ways. A row of interrupted



Fig. 7a

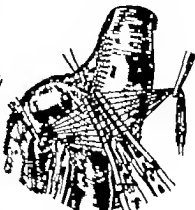


Fig. 7b

mattress sutures of silk is applied posteriorly the needle and suture paralleling the clamps as close as subsequent tying will permit. After all have been applied, they are tied.

A row of interrupted mattress silk sutures are applied anteriorly the needle and suture again paralleling the clamps (Fig. 7b). The clamps are removed and the stitches tied separately. A few additional sutures are applied at the two extremities of the stoma to insure a leak-proof closure. After the last stitch has been tied the new gastrojejunal stoma is opened by gentle digital manipulation.

This method of approximation of serosal surfaces for re-establishing intestinal continuity (Fig. 7) as used in our early aseptic resections, has been superseded in later resec-

tions by utilizing Martzloff's modification of the Parker Kerr basting stitch as suggested by Wangenstein. The clamps are rotated away from the proposed posterior line of closure. A continuous basting stitch of No. 0 chromic catgut on an atraumatic needle is applied alternately to the contiguous gastric and jejunal serosal surfaces lying posterior to the clamps (Fig. 8a).

The clamps are rotated toward the posterior suture and a second continuous Parker Kerr basting stitch of No. 0 chromic catgut is applied alternately to the contiguous gastric and jejunal surfaces lying anterior to the clamps (Fig. 8b). The clamps are removed, the two sutures pulled taut, thus accurately approximating the serosal surfaces posteriorly and



Fig. 8a

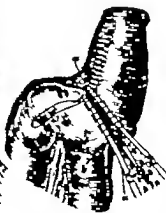


Fig. 8b



Fig. 8c

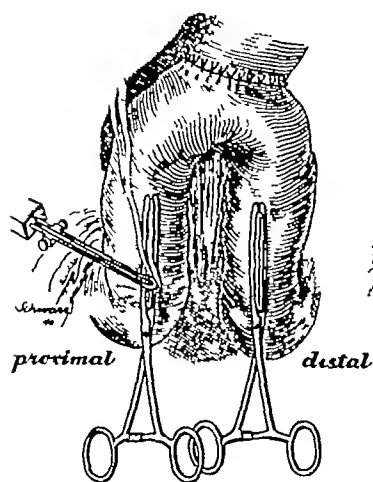


Fig 9a

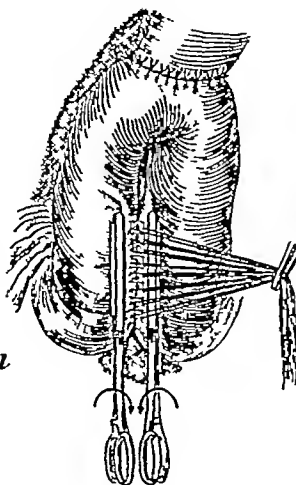


Fig 9b

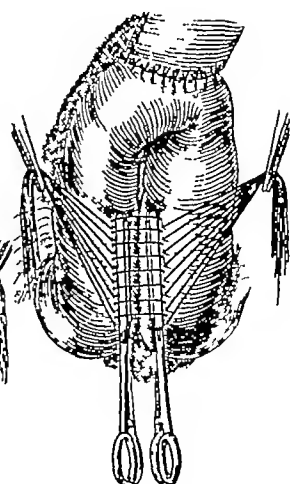


Fig 9c.

anteriorly The two sutures are tied together at each end (Fig 8c, a, b) This line of continuous catgut suture is in turn buried by interrupted silk sutures applied posteriorly and anteriorly Digital manipulation insures the opening of the stoma

In resections for ulcer in which a larger remnant of stomach remains than in resection for carcinoma, this completes the operation

The larger remnant of stomach following resection for ulcer does not recede into the left upper quadrant, and therefore obstructing angulation of either of the two jejunal arms of the gastrojejunal anastomosis is not so imminent The *anterior* gastrojejunostomy also contributes to diminishing the danger of such obstructing angulation Moreover, in resections for ulcer, a jejunojejunostomy between these two jejunal arms of the gastrojejunostomy is strictly avoided, as it is considered highly undesirable to deflect the alkaline duodenal and pancreatic secretions through an enteroenterostomy, away from the gastroenterostomy The neutralization, preferably in the stomach, of the acid gastric secretions by the alkaline duodenal secretions is most effective in preventing jejunal ulceration

In all cases of subtotal resections for cancer, in contrast to resection for ulcer, the anterior gastrojejunostomy with a complementary jejunojejunostomy is considered practically obligatory (Figs 9 and 10) It is our aim in resections for cancer to remove the entire

lesser curvature together with the gland bearing tissues in the gastrohepatic mesentery and most of the greater curvature The small remnant of stomach resulting from this procedure recedes high into the left upper quadrant, under the left diaphragm Were a posterior gastrojejunostomy performed through a rent in the mesocolon, a drag on the mesocolon would occur, and obstructing angulation of one or both arms of the jejunum would be imminent Even if this immediate danger were averted, the hazard of a jejunal ulcer or of a gastrojejunocolic fistula is greatly increased by tension on the anastomosis from a fixed or short mesocolon I propose as an axiom in gastric surgery that following any gastric anastomosis, the stomach must be *comfortable*, both at rest and in activity Any interference with the effective motility of the stomach, either by the fixed or short mesocolon or by the stomach being joined to the fixed portion of the jejunum, will surely lead to tragic consequences In resections for cancer, therefore, an anterior gastrojejunostomy is invariably performed and since there is no danger of jejunal ulceration incident to the deflection of the alkaline duodenal secretions away from the gastrojejunal anastomosis, an enteroenterostomy is also performed between the two arms of the jejunum leading to and from the gastric stoma Two thin-bladed Martzloff or Wangenstein crushing clamps are applied tangentially on the jejunal wall (Fig 9a), a segment

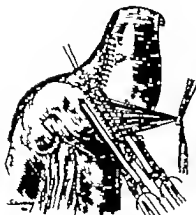


Fig. 7a.

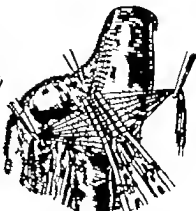


Fig. 7b.

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Fig. 8a.



Fig. 8b.



Fig. 8c.

HUMAN BITES OF THE HAND

HARRY MILLER, M D , and JAMES M WINFIELD, M D , F A C S ,
Detroit, Michigan

EXPERIENCE in many communities has yielded abundant proof of the danger which attends neglect of wounds contaminated with human mouth organisms. As the concomitant sequelae and resultant functional disturbances are often of a most serious nature, the importance of the correct management of the early and late human bite lesions cannot be over-emphasized. There is a definite tendency for these infections, when once established, to extend and to invade into deeper and more vital structures, the lesions rapidly becoming foul smelling, necrotizing, and resistant.

The organisms implanted in the tissues of the hand are often most virulent. The part played by such anaerobes as the fusiform bacillus and the spirochete of Vincent has been repeatedly pointed out. Although these organisms are not always demonstrable in cultures and smears from human bite wounds, dark field examination of fresh wet smears will demonstrate their presence in a higher percentage of instances. Anaerobic cultures observed over a period of 7 to 10 days will often yield much information. Streptococci and staphylococci alone and in symbiosis, as well as other contaminants such as the colon bacillus, various fungi and occasionally the *Spirocheta pallida* play an important rôle in producing and prolonging these necrotizing infections.

In order to gain a lucid concept of the problems involved in the prophylaxis and treatment of these lesions one must appreciate the anatomic complexity of the tissues which predisposes to extension of infection rather than to localization, particularly under conditions of neglect, as well as the low resistance of fibrous connective tissue and cartilage, to infection.

A knowledge of the mechanism of production, the usual sites of injury, the extent and

depth of the lesion, and the possible course of extension of the infection is of considerable aid in the intelligent management of these cases.

Human bite injuries usually occur during the course of fist fights or drunken biting brawls. Consequently, the lesions range from actual bites of the phalanges and hand to puncture wounds and lacerations produced by a fist striking exposed teeth. When the closed fist is used in striking a blow the knuckles of the second and third metacarpals receive the major force of the impact. This is primarily due to the fact that these bones are longer and stronger than the other metacarpals and, furthermore, they are more immobile. In this position the dorsal ligaments, extensor tendons, and skin are tightly stretched across the joint, and a blow on the projecting head of the metacarpal will easily cause a sharp, resisting surface to penetrate the joint cavity or to damage underlying structures (Fig 1).

A more rare mechanism, that of the sucking of hangnails or of clean lacerated wounds by the patient or a concerned bystander, will account for contamination with mouth organisms in a small number of cases. One of the patients included in our group of late infected cases acquired a severe infection following the biting of a hangnail.

In reviewing our early human bite wounds we have encountered almost twice as many lacerations of the fingers as of the knuckles. In the late cases the converse is true. The wounds of the phalanges occur predominantly on the dorsum, the palmar surface only occasionally being involved.

In regard to the extent and depth of the lesions, the injury may present itself as (1) a simple abrasion over the phalanges, knuckles, or palmar surface of the hand or wrist, involving only the epidermis (Fig 2), (2) a complete avulsion of segments of skin, subcutaneous structures and occasionally of bone (Fig 3), (3) a penetrating laceration either partially or completely severing the extensor tendon (Fig

From the Departments of Surgery, Wayne University College of Medicine and the Detroit Receiving Hospital.

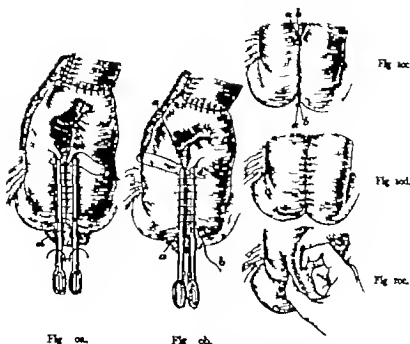


Fig. 9a.

Fig. 9b.

Fig. 10c.

Fig. 10d.

Fig. 10e.

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Any available omentum is brought up to lie between the under surface of the incision in the abdominal wall and the underlying viscera. The wound is closed in layers.

In numerous experimental anastomoses and in 31 clinical resections of the stomach for cancer and ulcer no hemorrhage has occurred or deaths, either from leakage or peritonitis. In not a single patient have we had an infection of the wound or evidence of a localized peritonitis.

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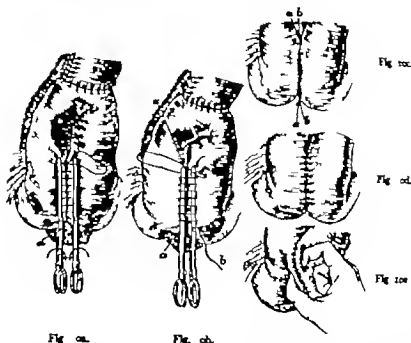


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The organisms implanted in the tissues of the hand are often most virulent. The part played by such anaerobes as the fusiform bacillus and the spirochete of Vincent has been repeatedly pointed out. Although these organisms are not always demonstrable in cultures and smears from human bite wounds, dark field examination of fresh wet smears will demonstrate their presence in a higher percentage of instances. Anaerobic cultures observed over a period of 7 to 10 days will often yield much information. Streptococci and staphylococci alone and in symbiosis, as well as other contaminants such as the colon bacillus, various fungi, and occasionally the *Spirocheta pallida* play an important rôle in producing and prolonging these necrotizing infections.

In order to gain a lucid concept of the problems involved in the prophylaxis and treatment of these lesions one must appreciate the anatomic complexity of the tissues which predisposes to extension of infection rather than to localization, particularly under conditions of neglect, as well as the low resistance of fibrous connective tissue and cartilage, to infection.

A knowledge of the mechanism of production, the usual sites of injury, the extent and

depth of the lesion, and the possible course of extension of the infection is of considerable aid in the intelligent management of these cases.

Human bite injuries usually occur during the course of fist fights or drunken biting brawls. Consequently, the lesions range from actual bites of the phalanges and hand to puncture wounds and lacerations produced by a fist striking exposed teeth. When the closed fist is used in striking a blow the knuckles of the second and third metacarpals receive the major force of the impact. This is primarily due to the fact that these bones are longer and stronger than the other metacarpals and, furthermore, they are more immobile. In this position the dorsal ligaments, extensor tendons, and skin are tightly stretched across the joint, and a blow on the projecting head of the metacarpal will easily cause a sharp, resisting surface to penetrate the joint cavity or to damage underlying structures (Fig 1).

A more rare mechanism, that of the sucking of hangnails or of clean lacerated wounds by the patient or a concerned bystander, will account for contamination with mouth organisms in a small number of cases. One of the patients included in our group of late infected cases acquired a severe infection following the biting of a hangnail.

In reviewing our early human bite wounds we have encountered almost twice as many lacerations of the fingers as of the knuckles. In the late cases the converse is true. The wounds of the phalanges occur predominantly on the dorsum, the palmar surface only occasionally being involved.

In regard to the extent and depth of the lesions, the injury may present itself as (1) a simple abrasion over the phalanges, knuckles, or palmar surface of the hand or wrist, involving only the epidermis (Fig 2), (2) a complete avulsion of segments of skin, subcutaneous structures and occasionally of bone (Fig 3), (3) a penetrating laceration either partially or completely severing the extensor tendon (Fig

From the Departments of Surgery, Wayne University College of Medicine and the Detroit Receiving Hospital.

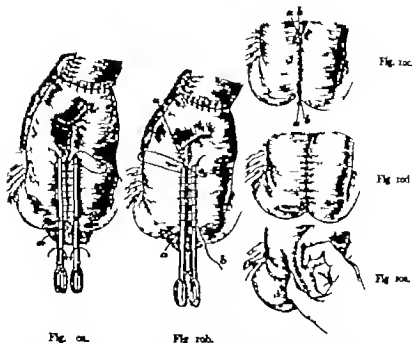


Fig. 9a.

Fig. 9b.

Fig. 10c.

Fig. 10d.

Fig. 10e.

of bowel wall is removed by the cautery the edges are secured for control of bleeding and an anastomosis is effected by one of two methods (x) by interrupted mattress silk sutures applied posteriorly and anteriorly parallel to the clamps (Fig 9b and c) or (y) by the Martzloff application of the Parker Kerr basting stitch (Fig 10d and e) The latter procedure is now considered preferable. A continuous No. 0 chromic catgut suture is applied paralleling the clamps posteriorly the suture passing alternately from one jejunal wall to the contiguous surface of the other (Fig 10a) The posterior suture remains loose while the clamps are rotated and a similar continuous suture of No. 0 chromic catgut is applied, paralleling the clamps anteriorly (Fig 10b) The two clamps are removed, and both sutures are pulled taut, thus approximating the apposed serosal surfaces and inverting the raw edges of the jejunum into the lumen (Fig 10c, a-b) These two catgut sutures are tied at both ends without puckering and without reducing the size of the anastomotic opening The entire anastomosis is reinforced

with interrupted silk sutures (Fig 10d) Digital manipulation insures opening of the stoma (Fig 10e)

Any available omentum is brought up to lie between the under surface of the incision in the abdominal wall and the underlying viscera. The wound is closed in layers.

In numerous experimental anastomoses and in 31 clinical resections of the stomach for cancer and ulcer no hemorrhage has occurred or deaths either from leakage or peritonitis. In not a single patient have we had an infection of the wound or evidence of a localized peritonitis.

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HUMAN BITES OF THE HAND

HARRY MILLER, M D , and JAMES M WINFIELD, M D , F A C S ,
Detroit, Michigan

EXPERIENCE in many communities has yielded abundant proof of the danger which attends neglect of wounds contaminated with human mouth organisms. As the concomitant sequelae and resultant functional disturbances are often of a most serious nature, the importance of the correct management of the early and late human bite lesions cannot be overemphasized. There is a definite tendency for these infections, when once established, to extend and to invade into deeper and more vital structures, the lesions rapidly becoming foul smelling, necrotizing, and resistant.

The organisms implanted in the tissues of the hand are often most virulent. The part played by such anaerobes as the fusiform bacillus and the spirochete of Vincent has been repeatedly pointed out. Although these organisms are not always demonstrable in cultures and smears from human bite wounds, dark field examination of fresh wet smears will demonstrate their presence in a higher percentage of instances. Anaerobic cultures observed over a period of 7 to 10 days will often yield much information. Streptococci and staphylococci alone and in symbiosis, as well as other contaminants such as the colon bacillus, various fungi, and occasionally the *Spirocheta pallida* play an important rôle in producing and prolonging these necrotizing infections.

In order to gain a lucid concept of the problems involved in the prophylaxis and treatment of these lesions one must appreciate the anatomic complexity of the tissues which predisposes to extension of infection rather than to localization, particularly under conditions of neglect, as well as the low resistance of fibrous connective tissue and cartilage, to infection.

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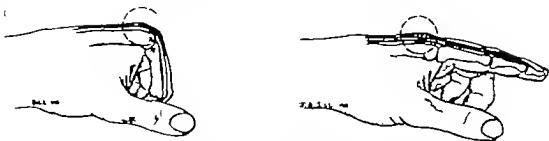


Fig. Region of knuckle. Mechanism of injury and implantation of infection.

4) (4) a wound which may have opened into the dorsal subcutaneous space subtendinous bursa dorsal subaponeurotic space or the joint cavity (Fig 5)

In 1930 Mason and Koch published a paper on human bite infections of the hand in which they demonstrated experimentally the lines of spread of infectious agents from the region of the metacarpophalangeal joint. This paper has been unsurpassed in the presentation of essentials and remains the outstanding contribution on this subject.

Obviously abrasions and avulsion lacerations offer little opportunity for the establishment of an anaerobic infection. Lacerations, however which have penetrated the subcutaneous layers and opened into the subtendinous tissues and joints, present ideal conditions for the production of fetid necrotizing infections because of the relatively anaerobic conditions, the low resistance of fibrous tissue and synovial membranes the anatomic complexity of structures favoring the spread of infection and the presence of traumatized



Fig 2.



Fig 3.



Fig 4.

tissue. Consequently, the infections occurring on the dorsal aspect of the hand in and about the metacarpophalangeal joint potentially and actually carry the graver prognosis. Because of the shift of tissues particularly about the knuckles, infection may be carried from an original point of entrance to a relatively distant area (Fig 1).

Infection occurring from an injury over the proximal phalanx may extend both superficial and deep to the expansion of the extensor tendon (Fig 6a). From this position it may extend along the lumbrical and interosseous tendons to involve the lumbrical space.

Laceration of the extensor tendon with the implantation of infection but without penetration into the joint may occur. Here the extension of infection will be extracapsular and subtendinous, the subtendinous bursa and subaponeurotic space becoming contaminated (Fig 6a). Should the joint be infected, infection may penetrate into the subtendinous bursa and subaponeurotic space as well as under the expansion of the extensor tendon over the proximal phalanx (Fig 6b) from which point infection will travel, as described, namely, to the lumbrical canal and large fascial spaces in the palm of the hand (Fig 7).

The dorsal subcutaneous space is usually involved early. This follows subcutaneous penetration with or without laceration or displacement of the tendon or extension into the joint.

The flexor tendons and their synovial sheaths are rarely invaded from behind. A dense fibrous sheath and the accessory volar ligament serve as an adequate barrier. Late in the course of infection, especially in neglected cases, the flexor tendon sheaths may be invaded.

Believing the results obtained by those surgeons using chemical and electrocautery



Fig 5 Penetration of the joint cavity

methods in the primary treatment of early human contaminated wounds are not entirely satisfactory (1, 2, 3, 5, 8), we have followed in our clinic the suggestion made by Mason and Koch in 1930 of cleansing the wound with soap and water combined with gentle débridement. The recognition of early human bites as such is often quite difficult. Falsification of history is common especially in the white patient, and often results in contraindicated primary suture. A definite and comprehensive regimen has been developed, comprising a searching history, complete examination, and treatment.

The routine treatment employed is as follows. The area about the wound is gently washed with soap and water for 5 minutes following which the wound itself is thoroughly washed with soap and water and irrigated with saline for a further period of 10 minutes. Following this procedure, the edges are gently retracted and the lesion examined, in order to determine the extent of injury if possible. These wounds are not probed since the information obtained is meager and the danger of carrying infectious agents more deeply into the tissues is great. Following mechanical cleansing and a very limited débridement, wet dressings are applied. No attempts are made to repair the rent in the joint capsule. Hands are splinted in the position of function. Lacerations are never sutured nor are injuries to

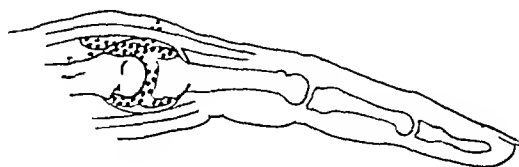
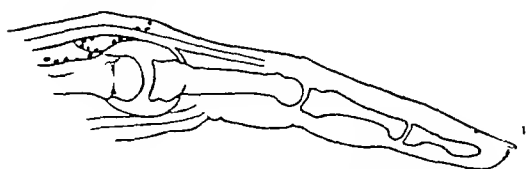


Fig 6 a, left, Extracapsular infection b, Intracapsular infection and extension

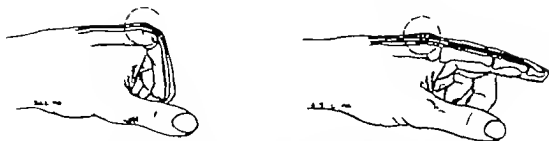


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Fig. 2

Fig. 2. Abrasion injury



Fig. 3



Fig. 4

Fig. 4. Penetrating laceration. Partial severance of

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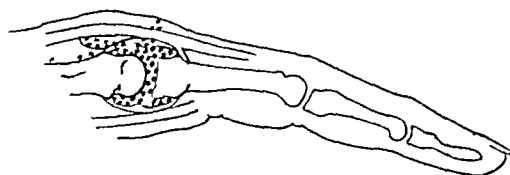
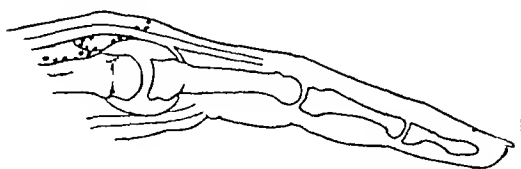


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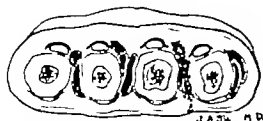


Fig. 7. Lumbrical space and palmar extension

deeper structures repaired. The major catastrophes in our series have occurred in those cases in which wounds were primarily sutured. Patients return daily for examination and if there is joint involvement, are usually hospitalized. In certain of the initial cases in this series patients were observed and treated in conjunction with Dr. R. E. Speers who has reported these previously. A total number of 61 early human bites of the hand have been given prophylactic treatment during the past 3 years. All patients seen within 4 hours after the occurrence of injury were considered early cases. Friedrich has pointed out that a lag phase of 6 hours exists before organisms contaminating a wound become acclimated to the human tissues. This lag phase in the case of organisms transferred from the human mouth is greatly shortened and there may be only a brief interval before the organisms are accustomed to their new environment. Those cases already presenting swelling and evidence of infectious extension were not included in this series of early cases even if patients were seen within the 4 hour period and were considered as late cases.

The accompanying table illustrates an interesting grouping of these injuries (Table I). It will be noted that 34 lesions involved the fingers while 18 occurred in the region of the knuckle. Of the total number of cases, 5 showed mild inflammatory reaction characterized by swelling and tenderness without suppuration and only 1 gave evidence of gross infection. Two of the knuckle injuries exhibiting inflammation had been sutured primarily due to falsification of history but the sutures were removed almost immediately and the wound treated as a human bite. One of the compound fractures with the tip of the ter-

TABLE I—EARLY HUMAN BITES OF THE HAND
(TREATED BY SOAP AND WATER WASHING,
LIMITED DÉBRIDEMENT, CALISTE IRRIGATION, WET DRESSINGS)

Location of injury	No. of cases	Remained clean	Mild inflammation	Gross infection
Compound fractures of finger	6	5		
Finger	34	31		
Knuckle	18			
Palm				
Dorsum				
Total	64	5		

*One additional case with extensive multiple injuries of the 5th finger and dorsum of the hand became grossly infected.

mild inflammation (Fig. 3). The compound fractures were usually hospitalized for a short period. The case referred to in the footnote was a most extensive injury, the fifth finger having been almost completely bitten off at the base of the proximal phalanx, tooth injuries of the third and fourth metacarpophalangeal joints and 3 lacerations over the dorsum of the hand. It was necessary to remove the fifth finger. The third and fourth metacarpophalangeal joints became stiff and the dorsal skin sloughed requiring a subsequent graft. Obviously gross suppuration occurred in this hand but we were able to save the major portion of the hand and to obtain a fair functional result. In none of the early cases except the last mentioned was it necessary to resort to amputation.

A more complete analysis has been made of the last 27 cases. In this group 10 were knuckle injuries, 5 of these occurring on the third right knuckle and 1 on the third left knuckle. Two occurred on the second right knuckle. Of the 17 finger injuries the first, second and fifth right fingers were most commonly involved. There were 10 extensor tendon lacerations and 1 flexor tendon laceration. The metacarpophalangeal joint was known to be entered in 3 instances, but no doubt lacerations involving the joint were more frequent than this, as the positive determination of the extent of the injury in this region is often difficult to ascertain.

Over 60 per cent of the cases were between the ages of 15 and 25 years, 8 being males,

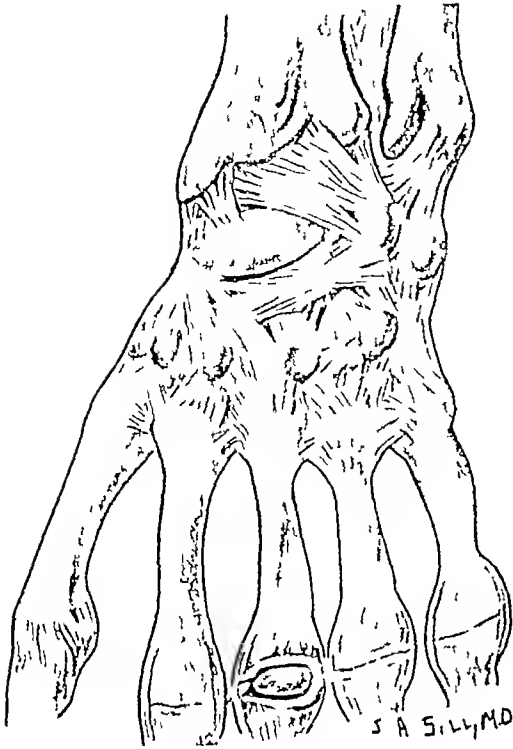


Fig 8 Usual type of incision for adequate joint drainage

9 females, 19 were colored, and 8 white. Of 22 cases the functional result in 20 was excellent, good in 1, and poor in 1 (cases described previously).

The average wound healing time for the whole series of 61 cases was 8.5 days and for the group of 27 cases 9.9 days.

The after-care consisted essentially of splinting and the application of continuous saline, boric acid, or magnesium sulphate soaks for a period of 48 hours. The wet dressings were discontinued at this time if the wounds remained clean. Splinting was continued to complete healing.

This relatively simple course of management of early human bite injuries has given results which have been most gratifying. Unfortunately, the patient, when first seen often has a fully established infection, and regardless of the adequacy of treatment, frequently is condemned to a prolonged illness which may result in loss of parts and occasionally in loss of life.



Fig 9 Healed incision. Drainage subcutaneous, subaponeurotic, and joint spaces

In marked contrast to the prophylactic treatment and management of the early human bite injuries, is the therapeutic problem presented by the late infected human bites. These wounds are already in serious conditions, and sometimes extensively infected. As in other infections of this type, adequate surgery is essential with emphasis on somewhat earlier and more radical drainage. In general, the basic principles enunciated by Kanavel, Koch, Mason, and others relative to the treatment of established hand infections should be adhered to scrupulously. It should be unnecessary and is obviously impractical to outline the treatment in the most minute detail. Suffice it to say, that under general anesthesia, and in a bloodless field, the hand is thoroughly cleansed with soap and water. Then an extremely careful, meticulous débridement is performed, with removal of as much infected, gangrenous sloughing tissue as possible, and in addition with adequate drainage for all areas of infection. Definite mention should be made regarding metacarpophalangeal joint infections. The joint capsule should be opened transversely by a 1 to a 1.5 centimeter incision which usually gives sufficient drainage (Fig 8). As has been pointed out earlier in the

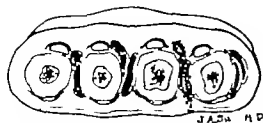


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WET DRESSINGS)

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Over 60 per cent of the cases were between the ages of 5 and 25 years, 18 being males,



Fig 12 Incision for drainage of lumbrical space

sulphate solutions, we have utilized and rather favor the use of Dakin's solution, it being our impression that the wounds remained cleaner and that sloughs separated more readily with consequently better drainage when the latter solution was used. Hydrogen peroxide, potassium permanganate, and chromic acid solutions also were used without notable success. Zinc peroxide, arsenicals, and sulfanilamide did not produce strikingly favorable results. The fingers, hand, and arm are then splinted and put at rest in the position of function and whenever possible arranged so that the position will favor dependent drainage. It is our belief that practically without exception cases of this type should be hospitalized. A Wassermann should be done in all patients presenting human contaminated lesions.

As has been stated, the initial injuries in the late infected cases occurring in the region of the knuckle outnumbered those of the fingers. In 34 of the 54 patients the knuckles were involved, 15 occurring over the third metacarpophalangeal joint, the others scattered and of this group of 34 cases, the joint cavity itself was infected in 19 instances. There were 19 cases with lesions of the fingers, 16 injuries being on the dorsal surface, and 3 on the volar surface. In 6 cases the middle interphalangeal joint was infected and in 4 cases the distal interphalangeal joint was involved. As might be expected, partial or complete laceration of extensor tendons occurred in 18 cases and in only 6 cases were the flexor tendons partially severed. There was 1 case presenting a laceration of dorsum of the hand alone.

In several cases there was multiple involvement of joints, fascial spaces, and tendon sheaths. However, in 12 cases infection was confined to the dorsal subcutaneous space and



Fig 13 Severely infected finger. Amputation required

in 21 cases both the dorsal subcutaneous and dorsal subaponeurotic space was infected (Fig 11). Infection of the midpalmar space was present in 3 cases and this seems significant in that this space is not commonly involved in the usual hand infection. In 1 case infection extended from an involvement of the index flexor tendon and its sheath to the thenar space. In another case the ulnar, radial bursa, retroflexor space, and bones of the wrist and hand became so severely infected from a knuckle lesion that amputation through the forearm was required. From an original focus at the metacarpophalangeal joint, infection spread to the lumbrical spaces in 9 cases. Thirteen cases of the total 48 developed stiff fingers and in 5 cases amputation of parts was required, in 1 of which it was necessary to perform amputation through the forearm (Fig 13).

In spite of the severity of these infections, the average length of healing was 34 days and 9.4 was the average number of hospital days. No fatalities occurred in this group of cases.

As has been noted in the literature (6), these infections are prone to recurrence and frequent exacerbations. In our series there were 3 such instances, 1 in 3 weeks, 1 in 2 months, and 1 in 3 years' time.



Fig. Function obtained following drainage of infection of subcutaneous sub-synoviotomic and joint spaces.

paper infections of this type when implanted in certain regions may characteristically spread along certain lines to involve adjacent



Fig. Drained infection. Dorsal subcutaneous and sub-synoviotomic space.

or deeper structures. The deepest anatomic plane involved should be inspected, as the infection may spread along the lowermost plane (Fig. 9). Infection of the joint, if adequately drained, does not always result in a completely ankylosed joint as in many instances excellent function is obtained (Fig. 10). An understanding of the pathogenesis of the advance of infection is essential to the correct surgical management of these severe infections, since it is only by locating those areas of greatest potential danger and recognizing the presence of infection that the lesion can be intelligently and satisfactorily managed. One should be slow to amputate extensively infected fingers but extensive drainage of the soft parts is essential. Often a useful part may be preserved or if amputation later becomes necessary more of the extremity may be saved. Amputation should be avoided in the presence of an acute infection.

The wounds are then loosely packed with vaseline gauze and usually massive wet dressings are applied. A considerable variety of antiseptic solutions have been employed. In addition to saline, boric acid and magnesium

INTERSCAPULOTHORACIC AMPUTATION FOR MALIGNANT TUMORS OF THE UPPER EXTREMITY

A Report of Thirty-one Consecutive Cases

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INTERSCAPULOTHORACIC amputation is an operation devised to remove the entire upper extremity, the shoulder girdle, and its muscular attachments. The operation has been variously designated as "removal of one-half of the shoulder girdle" by von Eiselsberg, "surgical removal of the breast girdle" by Adelman and "extirpation of the arm and shoulder" by Kocher, but it is the term "interscapulothoracic amputation" which the French surgeons, notably Berger, have employed and which now enjoys popular usage.

In the *Anatomy of the Human Body* by W. Cheselden, there is a note and illustration concerning the case of Samuel Wood, a miller, who in 1737 survived a traumatic amputation of an arm and shoulder, caused by an entwined rope attached to the cogs of a mill wheel. Only slight shock was said to have followed this amputation by avulsion. The English surgeon, R. Cumming, has been generally accredited with having performed the first elective operation of this type which was for a gunshot wound, although Halstead maintained that Larrey was the originator of the formal procedure, as it is done today. Dixie Crosby, in 1836, was the first American surgeon to perform a successful extirpation of the shoulder girdle for tumor. In 1837, Musey of Cincinnati did a scapulectomy following a disarticulation of the humerus for sarcoma, the patient survived 30 years.

Until 1881, i.e., before the era of antiseptics, there were 29 recorded interscapulothoracic amputations for various indications, with an operative mortality of 38 per cent.

The technique of the operation was standardized by Berger, and the classical procedure still bears his eponym, in 1887 he described all the previously published cases and added his own experience with the operation, for which his mortality rate was 10.4 per cent. The most important article dealing with this subject in medical literature was written by Buchanan of Pittsburgh, who analyzed all the reported cases prior to the year 1900. At that time the operation was so unusual as to be a surgical curiosity and surgeons were inclined to rush their individual case reports into press before final end-results could be appreciated. Buchanan, by letter and consultation, secured most of the follow-up data on 141 interscapulothoracic amputations which were done prior to the year 1900.

Our analysis of the evolution of this operation, the indications, and contraindications for it, the modifications of techniques employed, and the final end-results achieved will therefore be presented in three parts: (a) A summary of the Buchanan report, which is a thorough analysis of 141 operations done prior to 1900 (Table II). (b) An analysis of 180 additional case reports from the medical literature from 1900 to date (Table III). This would indicate that the operation is done with surprising infrequency. A complete bibliography of 357 references originally appended to this article revealed the fact that the operation is universally done. These references to articles which appeared in Russian, Japanese, Swedish, Dutch, Portuguese, Italian, Spanish, Hungarian, Roumanian, and Polish medical literature have necessarily been deleted from this article because of insufficient space. Russian surgeons as a national group have probably applied this radical procedure more often than others and, moreover, have contributed

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Since instituting the described management of early human bite lesions, the number of late cases admitted to the hospital have been definitely fewer in number. For a short interval during a change in the resident staff the late infected cases increased and it was found that the treatment of the early cases was not being carried out as outlined.

The careful evaluation of results in the treatment of human bite infections is difficult because of the variations in the virulence of the contaminating organisms and the resistance of tissues. The criterion of the length of stay in the hospital is not a good index of the extent or severity of the infection. These studies have convinced us that good results in the treatment of human bite infections of the hands can be obtained only by attention to details and adherence to surgical principles. Careful cleansing and gentle handling of tissues have reduced our incidence of severe infections and adequate drainage fixation of parts and irrigation are fundamental necessities in the treatment of the late infections.

SUMMARY

1. The prophylactic treatment of early human bite injuries handled under the reg-

men of soap and water cleansing, limited debridement, wet dressings, and splinting is simple and effective the results obtained being superior or equal to those attained when actual or chemical cauterization was utilized.

2. The correct management of the early human bite cases has reduced the number of late infected cases and we feel that prompt and intelligent treatment of the infected cases has definitely reduced the morbidity and number of disabling and deforming sequelae.

3. In dealing with the late infected cases a clear understanding of the mechanism, depth of penetration and degree of injury in relation to the spread of established infection is essential for adequate and correct surgical treatment.

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TABLE III — SUMMARY OF REPORTED CASES
IN MEDICAL LITERATURE—1900 TO DATE

	Cases
Sex	
Male	123
Female	50
Sex not stated	7
Total	180
Youngest 2½ yrs, oldest 72 yrs, average, 30½ years	

Age by decades	Cases	Cases
0-10	6	41-50
11-20	37	51-60
21-30	20	61-70
31-40	33	71-80

	Cases		Cases
Pathological diagnoses			
Osteogenic sarcoma	41	Spindle cell sarcoma	14
Chondrosarcoma	11	Neurosarcoma	7
Chondroma	8	Schwannoma	1
Myeloid sarcoma—bone	5	Rhabdomyosarcoma	1
Giant cell "sarcoma"—bone	7	Angiosarcoma	1
Lymphosarcoma—bone	1	Perithelioma	2
Endothelial myeloma	1	Sarcoma unclassified	38
Round cell sarcoma	15	Melanoma	1
Lymphosarcoma	1	Squamous cell cancer	6
Mixed cell sarcoma	6	Adenocarcinoma of breast and axilla	6
Myxosarcoma	1	Malignant tumor unclassified	3
		Diagnosis not stated	4

Location of tumor	Cases		Cases
Humerus and upper arm	95	Soft parts—shoulder	7
Scapula	24	Axilla	9
Clavicle	2	Carcinoma of arm and shoulder	5
Scapula and clavicle	6	Recurrent cancer of breast	4
Scapula and humerus	9	Location not stated	1
Clavicle and humerus	3	Secondary involve ment of shoulder joint	22
Clavicle, scapula and upper arm	7		
Shoulder joint	8		

Previous operations ¹	Cases
Radical mastectomy	5
Resection of humerus	2
Shoulder joint disarticulation	5
Amputation of arm	2
Excision—cancer in burn scar	2
Formal incisional biopsy	5
Local excision of tumor	30

Method of interscapulothoracic amputation	Cases
Typical Berger technique	115
Le Conte modification (Elliot, Harrington, Vaughan, Jeanbrau)	11
Kocher anterior approach (Powers, Lund, Brin, Murphy, Pomonorov)	7
Littlewood posterior approach (Sondermayer, Parakh)	2
Conjoined radical mastectomy (Cushing, Fischer)	2
Kuster method (Knierrn, Troitzky)	2
Method not stated	41

TABLE III — Continued

	No	Per cent
End results—180 cases (collected)		
Operative deaths	9	5
Lost to follow up	78	43 3
Dead		
From local recurrence	12	6 7
From pulmonary metastasis	31	17 3
From intercurrent diseases	7	3 9
Total	50	27 7
Living ²		
With recurrence	5	2 8
Without disease	38	21 2
Total	43	23 9

Of the 34 patients with malignant tumors, living and well and remaining under observation, the average post operative survival period was 16 2 months. The distribution of survival periods was as follows:

0-6 mos	16
7-12 mos	3
1-2 yrs	5
2-3 yrs	8
3-4 yrs	0
Over 4 yrs	2

¹Fifty-one of the 180 patients had undergone other operations prior to the interscapulothoracic amputation. Of these 35 patients had 1 operation, 7 had 2, 4 had 3, 3 had 4, 1 had 5, and 1 had 6 previous operations. The types of previous operations are listed.

²Of the living patients, 4 had benign tumors (chondromas) and were known to be living and well for 6 months, 7 years, 12 years, and 27 years respectively following the interscapulothoracic amputation.

geon's viewpoint. The ultimate psychological effect of this operation on our patients has not been bad, those who are living are apparently happily adjusted to this handicap.

The indications for this operation may be enumerated in the following decalogue:

1 Non-neoplastic conditions, such as extensive trauma with irreparable damage, gunshot wounds, tuberculosis, incurable osteomyelitis. It is not the purpose of this critique to discuss these indications at length.

2 Intractable pain caused by incurable tumors of the shoulder girdle even though metastases to lungs are present. The purpose here is palliation only, in getting rid of a cumbersome, painful, often suppurating extremity (Polosson, Jeanbrau). This indication is not so valid now that intolerable pain in the shoulder and arm can often be controlled by such neurosurgical measures as cervical chordotomy and posterior rhizotomy.

3 All malignant tumors requiring disarticulation of the humerus at the shoulder. The more major procedure in our experience does not require the penalty of a higher operative

TABLE I.—COMPARATIVE END-RESULTS OF SCAPULECTOMY AND INTERSCAPULOTHORACIC AMPUTATION—KAWAMURA (1909)

	Total No.	Survivors		Operative deaths	
		No.	Percent	No.	Percent
1. Laparoscopic scapulectomy	20	14	85	6	30
Complete scapulectomy	66	39	59	27	41
	94		84		7
Interscapulothoracic amputation	27	20	74	7	26

some interesting modifications of the operation (Tikhov Sapezhko Ilchenko) (c) A report of 31 personal cases from the bone and mixed tumors services of the Memorial Hospital (Table IV). These 31 unselected, consecutive interscapulothoracic amputations were all done for malignant tumors of the upper extremity and were performed without an operative death.

INDICATIONS FOR INTERSCAPULOTHORACIC AMPUTATION

The necessity for performing such a massive, disabling and disfiguring amputation demands a clear conception of the indications, hazards, natural history of the tumor, responsible and possible end results to be achieved. The idea of sacrificing the clavicle, scapula, and arm with their muscular attachments is so repugnant to most patients and repellent to many surgeons, that one of three sequences is apt to follow: The patient refuses with finality all operative aid, or accepts a more conservative though less certain treatment, or eventually agrees after a prolonged interval, during which the disease advances to the stage wherein an operation of desperation is substituted for what was originally an operation of hope. It may be said in all fairness to the operation which is unquestionably well conceived that too few of them are done as carefully planned elective initial procedures and too many are performed as a last resort following one or more recurrences after incomplete or more conservative operations. The indetermination or reluctance of the patient is not a contraindication from the sur-

TABLE II.—BUCHANAN'S ANALYSIS OF END-RESULTS, PRIOR TO 1900

Sex	Male	Female	Not given	Total	Age by decades	to 10	10 to 20	20 to 30	30 to 40	40 to 50	50 to 60	60 to 70	70 to 80
Cases	11	39	9	59									
Operative deaths	1	1	0	2									
Pathological diagnoses													
Sarcoma, unclassified	05	Cardioma	7										
Malignant tumor, unclassified	5	Encephaloma											
Osteosarcoma		Medullary growth											
Chondrosarcoma	3	Cystoid growth											
Myxosarcoma	4	Chondroma	7										
Lymphosarcoma		Basaloma tumor											
Location of tumor													
Humerus and upper arm	35	Soft parts—shoulder											
Scapula	24	Axilla	4										
Clavicle joint		Carcinoma of shoulder											
Shoulder joint		Recurrent cancer of breast	4										
Humerus and scapula	5	Location not stated	12										
Clavicle and scapula	3	Secondary involvement of shoulder joint											
Clavicle and humerus	3												
Clavicle, scapula and humerus	6												
Operative deaths—	3 per cent												
Cause													
Shock	7	Location of tumor											
Hemorrhage		Upper arm	3										
Infection		Scapula (alone)	3										
Other causes	6	Shoulder	3										
		Breast											
		Location not stated	4										
End results													
Total	89	Total	44										
to 6 mos	27	Dead	7										
7 to 12 mos	20	With disease	6										
3 to 24 mos	8	Without disease	3										
1 to 3 yrs	3		3										
3 to 4 yrs	3												
4 to 5 yrs													
5 to 7 yrs													
to 20 yrs	4		3										
to 30 yrs													
Cause of death													
Operative deaths													
Local recurrences													
Pulmonary metastasis													
Not stated													

Scope of above operable carcinoma tumors were removed G.C. Wall of Adipose removed one weighing 21 pounds and Shapard of Montreal removed one which was 30 inches in circumference



Fig 9 Case 15 Operative specimen of amputated hand and forearm. Note congenital neurogenic contractures of fingers associated with localized neurofibromatosis of this extremity. Multiple neurosarcomas appeared, first of hand, later of forearm (see cut), later of upper arm and finally of shoulder, necessitating interscapulothoracic amputation.

The arm is then drawn across the body and the posterior flap is outlined by an incision of the skin along the vertebral border of the scapula, which unites with the anterior incision along the lateral axillary border. The arm is then swung back to its original position and the anterior incision is deepened as far as the pectoral muscles. Division of the pectoral muscles now gives an excellent exposure of the brachial plexus. The surface of the plexus is painted with 10 per cent cocaine and/or 2 per cent novocain solution is injected into the nerve trunks. After division of the various



Fig 10 Case 15 To illustrate the anatomical defect and character of the scar. This patient is now living and well more than 6 years following this operation for neurogenic sarcoma.

nerve components of the plexus, the ligated proximal stumps are injected with small quantities of 95 per cent alcohol to lessen the possibility of amputation neuromas and causalgia. The arm is now brought forward again and the muscles of the posterior flap, along the vertebral margin of the scapula, are divided. Care is taken to clamp, sever, and ligate the transverse cervical artery before it retracts, if this has not been done at an earlier stage. With the scapula freed of its muscular attachments, the amputation is complete. The bleeding vessels are ligated with fine silk. The skin can usually be closed with interrupted black silk sutures. It heals with a surprisingly good linear scar. Since the adoption of the silk technique there has been less need for the use of drains. Skin grafting is resorted to in instances in which the size and the location of the tumor and the degree of skin involvement require a greater sacrifice of skin.

The patient is usually able to be out of bed on the third postoperative day and home

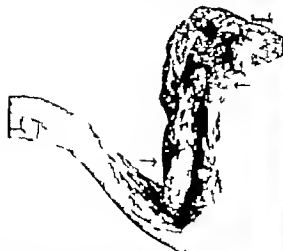


Fig. 7. Case 7. Malignant melanoma, primary on the hand with metastases to epitrochlear and axillary lymph nodes and diffuse linear extension by permeation through the arm. Gross specimen shows extent of involvement. The mass in the upper arm is almost microscopically indistinguishable from neurosarcoma.

with preservation of the arm, if involved by chondrosarcoma or osteosarcoma of low grade malignancy.

10. Relatively benign tumors causing symptoms and disability because of their size and location e.g. certain huge chondromas developing in the neighborhood of the shoulder joint.

OPERATIVE TECHNIQUE

A. The Classical Berger Operation

The patient is placed on his back with the involved shoulder elevated so that the skin can be prepared by antisepsis well beyond the midline front and back. The corresponding arm is well wrapped from fingers to shoulder and left free and mobile to be held by an assistant. By this means the arm may be held in various positions to facilitate the anterior or posterior dissection of the shoulder. Tournequet and Wyeth pins are unnecessary.

A linear incision is first made over the middle third of the clavicle and this incision is extended through the soft tissues to the periosteum. The middle third of the clavicle is now resected, usually with a Gigli saw. Through this window the subclavian vessels are exposed with the artery more deeply



Fig. 8. Clinical photograph of tumor suitable for interscapulothoracic amputation. Osteosarcoma developing on base of Peyer's disease of bone, Case (see Table IV).

situated beneath the vein. At this point the modification of LeConte may well be given, as he advocates the resection of the entire clavicle beginning with the sternoclavicular joint, for the avowed reason that this procedure does afford a better exposure of the subclavian vessels, particularly the artery which is to be ligated first, and it enables the operator to recognize and ligate the suprascapular and transverse cervical vessels. This complete claviclectomy does give better exposure and is absolutely indicated if the clavicle is involved by the tumor but it must be admitted that there are greater dangers of air embolism and injuries to the pleural dome and thoracic duct (on the left side).

After exposure of the neurovascular bundle at the base of the neck the subclavian artery is divided between ligatures of heavy black silk and the vein is treated in a similar manner. The proximal stump of the artery and vein are always doubly ligated. The original skin incision is then carried almost to the tip of the acromion after which it is extended downward along the anterior axillary border



Fig 13 Case 19 Left, Ulcerating, fungating neurogenic sarcoma of forearm, treated by amputation through upper arm. Recurrence later developed in the axilla, which was



then treated by interscapulothoracic amputation

Fig 14 Case 19 Character of wound 18 days after interscapulothoracic amputation

merus and then doing the scapulectomy later.

LaFaye did not resect the clavicle, but ligated the axillary vessels and disarticulated the humerus and the scapula from the clavicle.

Kuster added a vertical excision over the sternomastoid muscle to the handle of the racquet incision along the clavicle. He asserted that this gave a better exposure of the subclavian vessels and that it was particularly helpful in permitting primary ligation of the transverse cervical artery and vein.

COMPLICATIONS

Interscapulothoracic amputation is a radical, major, and dramatic operation, but it is really a simple and safe procedure once the subclavian vessels are securely ligated. The exposure of these vessels is occasionally very difficult due to the location of certain bulky tumors which overlie the operative field. In thin-chested individuals, especially when the arm has long been useless, the subclavian vessels as they lie on the first rib must be looked for considerably above the clavicular incision. With the danger of hemorrhage avoided, the patient subjected to this operation is relatively safe. In one of our recent patients, the subclavian vein was accidentally opened during a difficult attempt to free the artery, air was audibly aspirated into the vein, hemorrhage although great was controlled by compressing the vein with a finger against the first rib, and the patient went into shock. He

was restored by immediate transfusion as the vein was repaired and the operator allowed to proceed with the amputation. The patient recovered from this experience without any late complications. One of von Bergmann's patients died from hemorrhage caused by extension of the cancer around the subclavian vessels, this surgeon made a heroic effort to save his patient by tying off the superior vena cava.

Shock is minimal when proper preoperative and sustaining measures are in use, such as blood transfusions, usually given concurrently during the operation using the opposite arm or leg. Due to fixation of the tumor, the pleural cavity may be entered with the complications characteristic of pneumothorax. Injury to the thoracic duct by a left interscapulothoracic amputation may conceivably occur, but we have never seen or read of this occurrence.

CONSERVATIVE OPERATIONS VERSUS INTERSCAPULOTHORACIC AMPUTATION FOR MALIGNANT TUMORS

In the previous listing of indications for interscapulothoracic amputation, the comparative values of this radical procedure with more conservative operations have been considered. The practicability of the irradiation of certain liposarcomas and lymphosarcomas and the dissection of muscle groups containing encapsulated rhabdomyosarcomas and neuro-



Fig. left. Case 6. Roentgenogram of osteosarcoma developing in fractured bone cyst. Right persistent axo-malon.

Fig. 2. Case 6. Osteogenic sarcoma. Clinical photograph illustrating regional location of tumor necessitating interscapulothoracic amputation.

within 2 weeks. One of our patients had such good primary wound healing that she was able to start a 600 mile automobile trip on the ninth day after operation.

B The Anterior or Pectoral Approach of Kocher

The only difficulty encountered during the Berger operation is the exposure of the subclavian vessels. The anterior approach suggested by Kocher avoids this handicap and in our hands has proved to be a welcome modification of the original operation. After the middle third of the clavicle has been resected, the ligation of the subclavian vessels is postponed until the anterior incision is carried through the pectoral muscles into the axilla. This part of the dissection is similar to the same phase in a radical mastectomy as the axillary artery and vein come immediately into view. With the more adequate exposure afforded by enlargement of the operating field the subclavian vessels are more readily located and the underlying artery mobilized and li-

gated without the previous hazard of injuring the overlying vein.

From this point on, the operative technique is exactly similar to that described.

C The Posterior or Retroscapular Approach of Littlewood

According to some advocates, particularly Knaggs, the posterior approach of Littlewood may be done with greater speed and more anatomical exactness. After division of the middle third of the clavicle the posterior flap is outlined first and then the scapula is freed from its medial and superior muscular attachments. The supposed advantage of this technique is that when the neurovascular bundle is encountered from the posterior aspect, the subclavian artery appears first the vein second and the brachial plexus last in the exact order desired for ligation and severance.

D Additional Operative Details

Carro (1924) suggested a 2 stage operation in old patients, first disarticulating the hu-

END-RESULTS

In a comparative study of end-results grouped in periods of medical effort, the statistician must carefully analyze the collected data for sources of possible error. For example, the number of long term survivals of patients with "sarcoma" following interscapulothoracic amputation listed in Buchanan's report prior to 1900 is much greater than the number surviving in the series we have collected and which were reported from 1900 to date. The surgical technique, facilities for early diagnosis, and more detailed knowledge of the life history of these malignant tumors have unquestionably improved, and yet the same good end-results are not achieved. The explanation probably lies in correct histological classification and diagnosis, for example, giant cell "sarcoma" of bone is now more commonly referred to as benign giant cell tumor of bone.

Histological type of tumor in relation to age of patient. As the sarcomas which comprise the majority of tumors for which this operation is done, are more common in young adulthood, the average age of 33 years for these patients is what would be expected. Because the operation does not cause much surgical shock, it may be safely done in the case of elderly patients, if there are no other contraindications. The youngest patient was 12 years and the oldest patient was 72 years of age.

The average ages of patients with the different histological types of tumors for which this operation was done was with osteogenic sarcoma, 23 years, with other malignant bone tumors, 48 years, with neurogenic sarcoma, 38 years, with rhabdomyosarcoma, 52 years, with melanoma malignum, 40 years, and with squamous cell carcinoma, 63 years.

Eighteen of the 31 interscapulothoracic amputations were for malignant bone tumors. During the past 6 years, there has been a growing tendency at the Memorial Hospital to perform this operation more frequently for neurosarcomas and rhabdomyosarcomas of the upper arm and shoulder.

Duration of symptoms in relation to histological type of tumor (Memorial Hospital Series). The malignant tumors of the soft

somatic tissues, i.e., neurosarcomas, rhabdomyosarcomas, and soft part sarcomas of undetermined histogenesis, present a longer latent period between the date of the first symptoms and the interscapulothoracic amputation, than do the malignant bone tumors, not because of slower growth or lessened degree of malignancy but because the necessity for a radical surgical procedure does not seem so urgent. Patient and surgeon alike are more content to temporize with conservative measures if the sarcomas do not involve bone. Primary or immediate interscapulothoracic amputation is more likely to be acceptable and to be done for malignant tumors of bone than for sarcomas of the soft somatic tissues. For example, the duration of symptoms before this operation for the various histological types of tumors was for osteogenic sarcoma, 6 months, for other malignant tumors of bone, 4 months, for neurogenic sarcoma, 60 months, for rhabdomyosarcoma, 16 months, for other soft part sarcomas, 25 months, for squamous cell carcinoma, 36 months, and for malignant melanoma, 3 months.

Type of previous operation (Memorial Hospital Series). In our experience, the formal incisional biopsy of sarcomas is a dangerous operation and from the viewpoint of prognosis should almost be considered a major procedure. The so called local excisions of soft part sarcomas, as performed at the Memorial Hospital, are not enucleations but radical dissections with sacrifice of normal tissues surrounding the neoplasm. Thirteen, or 42 per cent, of our 31 patients had undergone previous operations, such as formal incisional biopsy, 5, local excision, 1, 2 excisions, 1, 3 excisions, 1, 5 excisions, 1, 7 excisions, 1, and lesser amputations, 2.

Type of operative technique (Memorial Hospital Series). Twenty-one of the interscapulothoracic amputations were done according to the Berger classical procedure. The 10 remaining operations were performed chiefly during the past 5 years by the Kocher anterior and pectoral approach which will undoubtedly gain favor because it can be performed with greater ease and safety.

Effect of preoperative irradiation on end-results (Memorial Hospital Series). Of the

sarcomas of low grade malignancy is recognized. One of us (B. L. C.) has published a series of case reports of scapulectomy for malignant tumors the osteochondrosarcomas of this bone may attain a large size without metastasizing. Although this operation has proved successful in the hands of some surgeons the cases should be properly selected. In an unbiased study of 65 malignant tumors of the scapula, Vancrède reported that not one patient had been cured by conservative measures.

In selecting one of these more conservative procedures such as scapulectomy or disarticulation of the humerus, the surgeon should do so with the firm belief that it is wholly sufficient as far as the local tumor is concerned and not because he relies on another opportunity for local cure through a secondary or subsequent interscapulothoracic amputation. (Table I)

The Tikhon-Linberg operation. An operation planned by the Russian surgeon Tikhon and applied afterward by Bauman and Linberg has for its purpose the excision of the scapula, clavicle and head of the humerus with preservation of an extremity which functions slightly. A racquet incision is made along the clavicle and the pectoral muscles are divided. The brachial nerve plexus and the subclavian artery and vein are dissected free and spared. A circular incision around the humerus determines the lower level of the resection and the humerus is sawed through. By a posterior incision over the scapula, this bone together with the clavicle and upper segment of the humerus is sawed through. By a posterior incision over the scapula, this bone together with the clavicle and upper segment of the humerus is resected. The biceps and triceps muscles are sutured to the intercostal muscles anteriorly and posteriorly. At the completion of the operation the lower arm, forearm, and hand are intact, and the functions of the forearm and hand are partly retained but of course shoulder and upper arm movements are no longer possible. A study of the case reports of this operation lends support to the belief that it is palliative only because the patients who have not died have required subsequent operations for recurrences.

ADVANTAGES OF INTERSCAPULOTHORACIC AMPUTATION OVER DISARTICULATION FOR MALIGNANT TUMORS OF THE UPPER ARM

The following advantages of interscapulothoracic amputation over disarticulation for malignant tumors of the upper arm may be mentioned:

- 1 The lymphatics and veins are removed at a much higher level.
- 2 The shoulder muscles with their natural fascial planes are entirely removed which is especially important if the tumor has shown invasive tendencies.
- 3 The more radical operation not only permits dissection of the axilla but a removal of the axillary boundaries.
- 4 The mortality is no greater. The 31 consecutive interscapulothoracic amputations reported in this article were done without an operative death which is proof enough of the safety of this operation.
- 5 The wounds resultant after interscapulothoracic amputation heal more satisfactorily as there are practically no dead spaces to be obliterated.
- 6 The deformity is greater but not enough to be a deciding factor.
- 7 Interscapulothoracic amputation is often done for a malignant tumor recurrent in the stump of the disarticulation. This very fact would indicate that the original disarticulation had not been wisely chosen as the proper operation. Consecutive operations finally terminating in interscapulothoracic amputation appear in every reported series, including our own (see Cases 15, 19 and 29 in Table IV). A patient with a neurosarcoma or fascial sarcoma of the hand, wrist, or forearm relates a history of one or more local excisions with recurrences developing each time proximal to the scar. Finally amputation of the forearm, later of the arm and still later disarticulation of the humerus may be done for proximally recurring tumors usually with increasing degrees of malignancy. Yet in retrospect for each individual patient in whom this series of events occurs, few surgeons would advise so radical a primary procedure as interscapulothoracic amputation for a sarcoma originating, for example, in the forearm.

TABLE IV—INTERSCAPULOTHORACIC AMPUTATIONS PERFORMED AT THE MEMORIAL HOSPITAL, NEW YORK, 1924-1940—Continued

Case Number	Date of operation	Age, yr	Duration of symptoms	Previous operations	Location	Histological type	Type of operation	Supplementary treatment		Cause of death		Post-operative duration	Comments on progress
								Preoperative	Post-operative	Metastases	Recurrence		
16 J B	3-25-35	31 M	10 yrs		Humerus	Medullary spindle cell osteogenic sarcoma	Berger					5 yrs 7 mos	Bone cyst with persistent non-union and growth one year prior to admission. Living with no evidence of disease
17 K H	9-15-35	12 F	2 yrs		Humerus	Osteogenic sarcoma	Berger pinch grafts	Radium element pack 200 kv x ray therapy Colby's toxins				5 yrs	No evidence of disease 4 months after operation
18 J C	7-22-36	15 M	2 mos		Humerus	Osteogenic sarcoma	Berger	200 kv x ray therapy	200 kv x ray therapy	Lungs	Yes	32 mos	Home on the 6th postoperative day. No evidence of disease for 3 months. Recurrence at 13 months after operation, treated with 200 kv x ray therapy and interstitial irradiation. Posterior rhizotomy for pain
19 W I	7-23-36	17 M	12 yrs	Blow and amputation of arm	Massive tumor recurrent in arm and axilla	Neurogenic sarcoma	Kocher			Lungs Skin			No evidence of disease 2 1/2 years after operation. Recurrence excised
20 J C	5-2-37	35 M	11 mos	Amputation biopsy	Scapula	Synovroma	Berger		200 kv x ray therapy	Lungs Pleum	Yes	3 1/2 yrs 3 mos	No evidence of disease 7 months after operation. Recurrence
21 V B	9-21-37	35 F	6 mos	Amputation biopsy	Humerus	Osteogenic sarcoma	Kocher	200 kv x ray therapy		Lungs		5 mos	
22 V C	9-29-37	2 M	11 1/2 mos	Amputation through arm	Humerus	Rhabdomyosarcoma	Berger	200 kv x ray therapy		Lungs	Yes	11 1/2 mos	No evidence of disease 7 months after operation. Recurrence
23 I R	11-20-37	20 M	10 mos	Amputation biopsy	Humerus	Osteogenic sarcoma	Berger			Lungs		23 mos	No evidence of disease 20 months after operation
24 I H	2-24-38	54 F	40 mos	Amputation biopsy	Upper arm	Rhabdomyosarcoma	Kocher	200 kv x ray therapy		Lungs		16 mos	No evidence of disease 15 months after operation
25 V C	3-2-38	11 M	21 mos	Biopsy	Upper arm	Neurogenic sarcoma	Kocher	200 kv x ray therapy		Lungs right buttocks		2 1/2 yrs	Living with no evidence of disease
26 V H	8-16-38	18 F	2 mos	Biopsy	Humerus	Rhabdomyosarcoma	Kocher		200 kv x ray therapy	Lungs		8 mos	No evidence of disease 4 months after operation. Ray therapy to metastases in right buttocks
27 F B	1-25-39	25 F	14 mos	Biopsy	Clavicle	Fibrosarcoma	Kocher	Radium element pack therapy		Lungs		8 mos	No evidence of disease 3 months after operation. Pregnancy complicated the case
28 I H	9-2-39	1 M	1 yrs	2 excisions	Axilla	Paraneoplasia	Kocher	200 kv x ray therapy (old radon seeds)				1 yr	Living with no evidence of disease
29 F S	11-4-39	30 M	5 yrs	5 excisions	Upper arm	Neurogenic sarcoma Grade III	Kocher					11 mos	Living with no evidence of disease
30 V S	2-2-40	17 M	6 mos		Humerus	Osteogenic sarcoma	Berger			Lungs		6 mos	No evidence of disease one month after operation. Living with recurrence and pulmonary metastases
31 W C	5-11-40	4 M	1 yr	2 excisions	Scapula and axilla	Rhabdomyosarcoma	Kocher pinch grafts	200 kv x ray therapy				4 mos	No evidence of disease one month after operation. Living with recurrence and pulmonary metastases

*Apoplexy.
Of 11 consecutive interscapulothoracic amputations performed at Memorial Hospital, 17 were done during past 6 years. With 3 exceptions operations were done by the authors on patients from bone and mixed tumor service.

TABLE IV—INTERSCAPULOTHORACIC AMPUTATIONS PERFORMED AT THE MEMORIAL HOSPITAL, NEW YORK, 1924-1940

Case Number	Date of operation	Age, years	Duration of illness, years	Previous operations	Location	Histological type	Type of operation	Supplementary treatment		Course of death		Post-operative duration	Comments on progress
								Preoperative	Postoperative	Mortality	Recovery		
L B	6-24	M	37		Apex, with carcinoma extending into axillary and no radiotherapy	Squamous carcinoma	Right thoracic amputation	Subtotal mastectomy, axillary lymph node dissection				37	Two operations for recurrence, 1927 and 1930. No evidence of disease 3-27-1933 6-12-33
G F	2-17-27	M	55	Lumpectomy	Scapula, axilla and neck	Neurogenic sarcoma	Right thoracic amputation	see by therapy		Yes		23 mos.	No evidence of disease for 6 months after operation
L V	12-27-27	M	50	Thoracic amputation	Apex, axilla and neck	Adenocarcinoma, transitional cell carcinoma, possibly squamous, possibly carcinoma of lymph nodes	Right thoracic amputation	see by therapy	Ovary's tumor	Long		mos.	
K W	7-22-28	M	47		Thoracic	Squamous carcinoma	Right thoracic amputation		Ovary's tumor, radical neck dissection	Long	Yes	37	No evidence of disease for 18 months after operation
K H	9-19-28	F	32		Thoracic	Squamous carcinoma	Right thoracic amputation	see by therapy		Long		37	
G B S	9-10-29	M	40		Thoracic	Squamous carcinoma	Right thoracic amputation	see by therapy		Long		37	
L V	9-13-29	M	40	Radical neck dissection	Apex, axilla	Melanoma	Right thoracic amputation		see by therapy	Long		mos.	
G J C	10-20-30	M	43		Thoracic	Phenol cell carcinoma	Right thoracic amputation			see by therapy		mos.	No evidence of disease for 16 months after operation
L V	10-20-30	M	44		Thoracic	Squamous carcinoma	Right thoracic amputation	see by therapy		see by therapy	Yes	mos.	
M J C	2-6-30	M	37		Thoracic	Squamous carcinoma on right	Right thoracic amputation	see by therapy		Long		16 mos.	
M J H	2-7-31	M	38	Right thoracic amputation	Thoracic	Squamous carcinoma	Right thoracic amputation	Ovary's tumor		Long		16 mos.	
B	6-17-31	M	43		Thoracic	Squamous carcinoma	Right thoracic amputation		see by therapy	Long		mos.	
G J O	10-20-31	M	40	Radical neck dissection	Thoracic	Squamous carcinoma	Right thoracic amputation	Ovary's tumor, radical neck dissection		Long		mos.	
H	1-2-32	M	44		Thoracic	Squamous carcinoma	Right thoracic amputation	see by therapy		Long	Yes	mos.	Postoperative recurrence in right thoracic area, 1933. No evidence of disease

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TABLE V.—END-RESULTS OF INTERSCAPULO-THORACIC AMPUTATION (MEMORIAL HOSPITAL SERIES)

End-results	No.	Per cent
Total cases	3	100
Dead		
From pulmonary metastasis.	5	48.4
From pulmonary metastasis and recurrence	4	9
From local recurrence.	3	9.7
From sarcomatosis.		3
From apoplexy		3
Total	24	77.4
Living		
With pulmonary metastasis	6	5
Without disease		9.4
Total	7	6

patients surviving at the time of this report, 2 who had no preoperative irradiation are clinically well for 21 and 67 months, respectively after the operation. Five patients who had preoperative irradiation are living: 1 with metastasis 4 months later and 4 without clinical evidence of recurrence for 20, 30, 60 months, respectively. Rocher and Papon assert that preliminary irradiation permits later interscapulothoracic amputation but no case reports were presented to support this contention. The application of irradiation as a means of avoiding this major amputation is a different matter entirely from the selective use of irradiation as a preoperative measure. It is different to evaluate the benefits of such therapy and it certainly cannot be done by a study of our own end-results, because we have been so liberal in giving x-ray and radium therapy to these patients. One would think

that interscapulothoracic amputation would suffice as the sole treatment if the line of incision were well above the upper limits of the tumor and that any preoperative adjuvant measures would be superfluous. Nevertheless, our past experience in dealing with sarcomas of the soft somatic tissues of other regions has indicated that there is greater freedom from local recurrence and distant metastases if preliminary irradiation is given. This is especially true for the liposarcomas. The reason for this is hard to fathom unless it could be that the trauma which is associated with the operation causes immediate dissemination of metastases; the lethal or abiotic action of the preliminary x-ray or radium therapy could conceivably lessen this hazard.

Patients living at the time of report (Table V). Of the osteogenic sarcoma group 2 patients were without disease 60 and 67 months, respectively, of the neurogenic sarcoma group 3 were without disease 11, 30 and 60 months, respectively, of the soft part sarcoma (undetermined histogenesis) group 1 was without disease 12 months and of the rhabdomyosarcoma group 1 was living with recurrence and pulmonary metastases, 4 months. The patient with squamous cell carcinoma lived 9 years without evidence of recurrence or metastasis and then died of apoplexy.

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TABLE VI.—POSTOPERATIVE DURATION IN RELATION TO TYPE OF TUMOR (MEMORIAL HOSPITAL SERIES)

Histological type of tumor	Number of cases	Postoperative duration in months	Range in months
Osteogenic sarcoma	5	8.5	5 to 67
Neurogenic sarcoma	5	3	to 60
Soft part sarcoma (undetermined histogenesis)	3	9.7	2 to 30
Malignant bone tumor other than osteogenic sarcoma	4	9.9	4 to 6
Rhabdomyosarcoma	1	0.5	
Squamous cell carcinoma	1	3	
Melanoma	1		
Malignant tumor unclassified	1		
Total cases	3	8	5 to 67

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in these experiments should be quite similar to those expected in man. The bacteriology of our experiments is summarized in Table I. Plain agar, blood agar, Endo's agar and anaerobic brain-heart infusion broth were routinely inoculated, and transfers to the various sugars were made as necessary to identify the individual organisms. The high incidence of *Clostridium welchii* leads one to the conclusion that had therapeutic serum been used, the mortality rate could have been lowered appreciably. This was the original intention of the authors, but Army reserve commissions interrupted the study (Table I).

There were 5 groups of 10 dogs each, 1 group of 12 dogs, and 1 group of 8 dogs. The results are tabulated in Table II and discussed more fully under individual experiments. The larger number of dogs in the bacteriological table is explained by the fact that many dogs died within 24 hours or that their wounds drained spontaneously and thus were discarded from the reported groups (Table II).

EXPERIMENT I

A control group of 10 dogs was established with a mortality rate of 100 per cent. This group consisted entirely of adult dogs whose wounds did not drain and who survived more than 24 hours. Dogs dying within 24 hours would not allow time for treatment and were, therefore, unsatisfactory for other experiments.

Dogs in this group were given food and water, as in all groups, but received no treatment. The wounds were opened in 24 hours for culture and then the mattress sutures were tied. These dogs all developed signs and symptoms of generalized peritonitis, characterized by leucocytosis, elevation of temperature, vomiting, and abdominal rigidity and tenderness. The average duration of life was 41.4 hours, most of the dogs died at 36 hours.

The standards agreed upon in the selection of this group were rigidly adhered to in all of the following experiments.

EXPERIMENT II

A group of 10 dogs was used in which treatment was started within 18 hours by an 0.8 per cent solution of sulfanilamide subcutaneously. One daily dose of 0.14 grams per kilo-

TABLE I.—BACTERIOLOGY OF EXPERIMENTALLY PRODUCED APPENDICEAL PERITONITIS IN 86 CONSECUTIVE DOGS

Organism	Dogs	Percentage
<i>Staphylococcus albus</i>	28	32.5
Anaerobic streptococcus	24	27.9
<i>Bacillus coli</i>	23	26.7
<i>Streptococcus fecalis</i>	3	3.4
<i>Clostridium welchii</i>	13	15.1
Gram positive rod of the <i>Listeria</i> group	11	12.8
Nonhemolytic streptococcus	6	6.9
<i>Staphylococcus aureus</i>	6	6.9
<i>Streptococcus viridans</i>	5	5.8
<i>Clostridium tetani</i>	3	3.4
<i>Proteus vulgaris</i>	2	2.3
<i>Staphylococcus citreus</i>	2	2.3
<i>Aerobacter aerogenes</i>	1	1.16
Gram negative rod of <i>Salmonella</i> group	1	1.16
<i>Sarcina lutea</i>	1	1.16
Anaerobic staphylococcus	1	1.16
Hemolytic streptococcus	1	1.16

gram of body weight was given in small amounts over the neck and back. Care was used not to overdilate the tissues in any one area, but in spite of this, most of the surviving animals developed skin sloughs. The average sulfanilamide blood level was 6.0 milligrams per cent and the highest obtained was 16.0 milligrams per cent. Of the dogs not surviving the experiment, the average duration of life was 55 hours. Autopsy showed no gross evidence of damage to the liver or kidneys but did show cloudy purulent peritoneal fluid and redness of peritoneum. The 5 surviving dogs (50 per cent) killed and subjected to postmortem examination later, showed only a few adhesions to the cecum and lateral wall.

EXPERIMENT III

Sulfanilamide (0.8 per cent solution) was administered intraperitoneally in 2 doses daily totaling 0.07 grams per kilogram of body weight. The dosage was reduced to 0.07 grams per kilogram of body weight because the first group of dogs given a dose of 0.14 grams per kilogram of body weight all expired within a few hours. Autopsy, however, failed to reveal any reason for the rapid death.

The drug was administered through a large bore needle which was found most convenient for these animals. Tubes sutured in place were pulled out by the animals, and drainage tracts resulted.

In this group the mortality rate was 50 per cent with an average survival of 38 hours. The

TREATMENT OF PERITONITIS

Intraperitoneal Use of the Sulfonamides Based Upon Animal Experiments

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THE bacteriostatic effect of the sulfonamides¹ is a well established fact in the mind of the clinician and the ever increasing literature serves to signify that this mode of action has a sound experimental basis while the details of its inhibitory effect are still in the theoretical stages.

In a very comprehensive article, Lockwood advances a hypothesis which supplies a theoretical framework upon which a complete scheme of sulfonamide chemotherapy may be constructed. He specifies the following 3 principal factors which should tend to modify the curative effect of the sulfonamide compounds: (1) concentration of the drug maintained in the immediate environment of the bacteria; (2) the mobilization of cellular defenses; (3) concentration of sulfonamide inhibitor substances. It is with the first factor that we find our chief interest in this experiment.

It is reasonable to believe that if the local concentration of the drug can be immediately elevated and maintained at the site of action of the invading organism or at an anatomical or pathological point the chances for a favorable outcome should be greatly superior to a route of administration which primarily promotes an elevated concentration systemically.

As to the ability to kill beta hemolytic streptococcus *in vitro* Colebrook, Buttle and O'Brien have definitely shown no essential difference between sulfanilamide laden blood from a treated patient and chemically treated blood from a normal individual.

Many workers (3-7-9) in various fields have endorsed the drugs as valuable for their local effectiveness. During the past year the attention of many abdominal surgeons has been

drawn to the possibilities of intraperitoneal use of the sulfonamides in the treatment of peritonitis. Thompson, Rosenberg, Dees, and others have reported the intraperitoneal use of crystalline sulfanilamide in the treatment of appendiceal peritonitis. It has been our experience from clinical and necropsy findings that powdered material in the peritoneal cavity is quickly walled off by omentum and is ultimately dependent upon absorption and systemic concentration for its local effect.

We have carried out a series of animal experiments in which we attempted a comparative study of the sulfonamides in solution or suspension by the systemic and local routes of administration.

In order to study this problem, it was necessary to produce an experimental appendiceal peritonitis comparable to that in man. The method described by Bower, Burns and Mengle (1) was used. The mesentery and base of the appendix were ligated and a large dose of castor oil was given to produce perforation and generalized peritonitis.

The wounds were sutured in layers, a small opening being left at the upper end where a through and through mattress suture was left untied. After 12 to 8 hours, the skin was prepared with iodine and alcohol and a sterile sponge forceps was introduced into the peritoneal cavity and rotated in a stirring motion to insure a generalized spread of the infection, and to a certain extent simulate the spread and trauma associated with the operation. Sterile applicators were then inserted for cultures and the mattress sutures were tied. Postmortem cultures were not taken because usually the animals had been dead an hour or two before being discovered.

As shown by Bower, Burns, and Mengle (2) the bacteriology is strikingly similar in man and dog and therefore, results obtained

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"Sulfonamide" is explained to include the three drugs of greatest current use: sulfanilamide, sulfapyridine, sulfathiazole.

in these experiments should be quite similar to those expected in man. The bacteriology of our experiments is summarized in Table I. Plain agar, blood agar, Lido's agar and anaerobic brain-heart infusion broth were routinely inoculated, and transfers to identify the individual organisms. The high incident of *Clostridium welchii* leads one to the conclusion that had therapeutic serum been used, the mortality rate could have been lowered appreciably. This was the original intention of the authors, but Army reserve commissions interrupted the study (Table I).

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The standards agreed upon in the selection of this group were rigidly adhered to in all of the following experiments.

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A group of 10 dogs was used in which treatment was started within 18 hours by an 0.8 per cent solution of sulfanilamide subcutaneously. One daily dose of 0.14 grams per kilo-

gram of body weight was given in small amounts over the neck and back. Care was used not to overdistend the tissues in any one area, but in spite of this, most of the surviving animals developed skin sloughs. The average sulfanilamide blood level was 6.0 milligrams per cent and the highest obtained was 16.0 milligrams per cent. Of the dogs not surviving the experiment, the average duration of life was 55 hours. Autopsy showed no gross evidence of damage to the liver or kidneys but did show cloudy purulent peritoneal fluid and redness of peritoneum. The 5 surviving dogs (50 per cent) killed and subjected to postmortem examination later, showed only a few adhesions to the cecum and lateral wall.

EXPERIMENT III

Sulfanilamide (0.8 per cent solution) was administered intraperitoneally in 2 doses daily totaling 0.07 grams per kilogram of body weight. The dosage was reduced to 0.07 grams per kilogram of body weight because the first group of dogs given a dose of 0.14 grams per kilogram of body weight all expired within a few hours. Autopsy, however, failed to reveal any reason for the rapid death.

The drug was administered through a large bore needle which was found most convenient for these animals. Tubes sutured in place were pulled out by the animals and drainage tracts resulted.

In this group the mortality rate was 50 per cent with an average survival of 58 hours. The

TABLE II.—COMPARATIVE STUDY OF SULFONAMIDES IN THE TREATMENT OF EXPERIMENTALLY PRODUCED APPENDICIZAL PERITONITIS IN DOGS

Experiments	Number of dogs	Number of deaths	Number of recoveries	Mortality per cent
I Control				100
II Sulfanilamide subq. 0.4 gm/kg		5	5	50
III Sulfanilamide, intraperitoneally 0.7 gm/kilogram daily divided doses		5	5	50
IV Sulfanilamide, intravenously 0.4 gm/kilogram daily divided doses		8		80
V Sod. Sulfapyridine, intraperitoneally 0.7 gm/kilogram daily divided doses		6	6	50
VI Sulfathiazole, intraperitoneally 14 gm./kilogram daily		4	6	40
VII Sulfabenzamide, intraperitoneally 14 gm./kilogram daily		8	7	87

highest blood level observed was 12 milligrams per cent, the average being 3.8 milligrams per cent. The peritoneal cavity of the dogs succumbing to the infection contained dark, greenish brown purulent fluid, sloughed appendices but no leakage from the cecum. The surviving dogs killed 2 weeks after cessation of treatment showed normal peritoneal cavities except for a moderate amount of free fluid which, in 2 cases was definitely bloody. The liver and kidneys were grossly normal.

EXPERIMENT IV

This group was treated with sulfanilamide (0.8 per cent solution) intravenously in 2 doses daily totaling 0.14 grams per kilogram of body weight. The mortality rate was 80 per cent with an average survival of 48.5 hours. The average blood level was 4.0 milligrams per cent.

The autopsy findings in this group were not significantly different from those of Experiment II.

EXPERIMENT V

Sodium sulfapyridine, 1 per cent solution was given this group of animals intraperitoneally in 2 doses daily totaling 0.07 grams per kilogram of body weight. The mortality rate was 50 per cent average survival 46 hours. The blood level in all the dogs 12 hours after dosing was below milligram per

cent. All dogs not surviving the experiment showed purulent fluid and generalized peritoneal inflammation. One abdomen contained a large amount of bloody fluid. Of the survivors, 2 showed very small omental abscesses (2 to 5 c.cm.) whereas the 3 others had normal peritoneal cavities with very few adhesions. No gross liver or kidney damage was observed in either group.

EXPERIMENT VI

Sulfathiazole being somewhat less soluble than the other sulfonamides, was given in 1 per cent solution and suspension, and it was so well tolerated that 2 doses daily totaling 0.14 grams per kilogram of body weight were given. The mortality of this group was 40 per cent the average survival time, 38 hours. The average sulfathiazole blood level was 4.3 milligrams per cent with 22.9 milligrams per cent the highest observed.

Postmortem examinations on death showed generalized peritonitis and purulent fluid. The appendices were sloughed in all cases yet the ligatures at the cecum held. Of the 6 surviving dogs killed 1 week later 2 had 300 to 500 cubic centimeters of bloody fluid with an injected peritoneum. The 4 other surviving dogs had very small omental abscesses containing about 5 cubic centimeters of purulent exudate at the ileocecal junction. Otherwise, the peritoneum was normal.

EXPERIMENT VII

In this group sulfabenzamide (4 N-caproamidobenzene-sulfonhydrazide) was dissolved in one tenth normal sodium hydroxide and neutralized with normal lactic acid. The resultant 1 per cent solution was nonirritating and according to Moore et al. is caproylamino-benzene-sulfonic acid which is thought by other observers to retain some therapeutic activity. Eight dogs were treated in this group by 2 intraperitoneal doses daily totaling 0.14 grams per kilogram of body weight. Seven, 87 per cent, of the 8 dogs died having 57 hours as an average survival time. The 12 hour blood levels in these dogs were all below 1 milligram per cent. The drug itself was not considered responsible for the deaths, as twice this dosage was given intraperitoneally as a single dose to normal animals with no apparent bad effects.

The necropsy findings of the succumbed animals were those of generalized peritonitis. Autopsy on one surviving dog showed only a few adhesions in the region of the cecum. Although the mortality rate does not speak well of the therapeutic efficacy of this drug, the experiment does eliminate the possibility of any of the animals in other experiments being saved by parenteral fluids rather than from specific action of the drugs administered.

ANALYSIS OF STUDY

The primary intention of this experiment was to determine the therapeutic value of the sulfonamides when applied locally in the treatment of peritonitis. Sulfanilamide was used as a standard to develop a safe and effective route of administration. The results as tabulated in Table II would seem to indicate that subcutaneous or intraperitoneal administration is preferable to the intravenous method. This is best explained by the relatively short action of the drug when given by the intravenous route.

Of the 4 drugs used intraperitoneally, sulfathiazole seems to be the most effective. This may in part be due to the fact that part of the drug was given in suspension which provided a longer time of action before complete absorption took place. We fully realize that the number of dogs in each group is too small for positive and definite conclusions, but we are certain that any one of the sulfonamides may be administered intraperitoneally with safety and without deleterious effect to the peritoneum or intraperitoneal organs. The usual toxic manifestations, of course, must be anticipated and treated appropriately if they arise.

Sulfanilamide intraperitoneally in the treatment of peritonitis seems definitely and unquestionably of value as proved by Mueller and by Jackson. In all of these cases, the drug was given in powder form. This necessitated a large initial dose, and any indicated subsequent intraperitoneal therapy with powder was difficult or was restricted to some other form and route of administration. Sodium sulfapyridine has been used intraperitoneally in a 4 per cent solution in 10 cases at The Oklahoma University Hospitals. The results

have been spectacular and the ease of administration remarkable. It can be given through the drainage tube in small divided doses or larger single doses, or by a continuous drip method, and repeated checks on the blood level can dictate the necessary dosage. In none of the cases in which the drug was given only by the intraperitoneal route were serious toxic manifestations encountered. There is evidence to indicate that combined therapy may be more hazardous.

CONCLUSIONS

- 1 Sulfanilamide, sodium sulfapyridine, or sulfathiazole may be administered intraperitoneally in solution or suspension in proper dosage, with no deleterious effect.

- 2 Intraperitoneal use of the sulfonamides is effective in the treatment of peritonitis.

- 3 Of the three sulfonamides, sulfathiazole appears to be the most effective in the local treatment of peritonitis.

- 4 Subcutaneous administration of sulfanilamide frequently resulted in skin sloughs.

- 5 Proper dosage is essential. The usual toxic manifestations may be expected and treated appropriately.

The authors wish to acknowledge the splendid cooperation of Ida Lucille Brown Wallace, instructor in the Department of Bacteriology, University of Oklahoma School of Medicine, who made the bacteriological studies in this experiment.

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RETROCECAL APPENDIX

Its Diagnosis and Surgical Approach

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THE single definite diagnostic feature of retrocecal appendicitis is a vertical line of tenderness starting at the iliac crest, 6 to 8 centimeters behind the anterior superior spine and extending vertically upward, the distance of the involved appendix, often to the rib margin.

The intensity of the initial symptoms is modified by the position. Both pain and vomiting are initially slower in their development and less intense in character. The appendicitis syndrome from the appendix situated retroceally can be compared to the syndrome of obstructive lesions of the lower bowel. The clinical picture of high bowel obstruction is similar to the freely placed acute appendicitis, while retrocecal appendicitis presents a clinical picture similar to that of lower bowel obstruction. Some systematic differential plan, as suggested by Sloan¹ should be borne in mind in confirming the general diagnosis of appendicitis before the search for localization is begun.

The following method of approach permits the removal of a retrocecal appendix with a minimum amount of contamination of the peritoneal surface.

The incision is made parallel to and about 5 centimeters lateral to the outer rectus margin, starting about 8 centimeters above the level of the umbilicus and following the outer margin of the rectus abdominis down to the level of the internal pillar of the external abdominal ring. This incision is curved with the convexity directed outward. The incision is carried down to the fascia of the external oblique; the fascia is exposed for the entire length of the skin incision (Fig. 1).

At the level of the anterior superior spine of the ilium and about 1 centimeter lateral to the border of the rectus muscle, the external oblique aponeurosis is incised vertically and

this incision is extended upward and downward to the limits of the skin incision (Fig. 2). The fibrous aponeurotic margins of the external oblique separated by the incision are held by hemostats as landmarks in closure (Fig. 3).

The internal oblique and transversus muscles are separated by blunt penetration with scissors to the preperitoneal fat, then by hooked digital retraction directed upward and downward are separated horizontally in the direction of their fibers, thus exposing the outer surface of the peritoneum and the preperitoneal fat. The under surface of the transversus muscle is now separated from the peritoneum below to the level of the inguinal ring above to the upper level of the incision, medially the peritoneum remains in its normal anatomic relation, but laterally and posteriorly from the iliac fossa, from the tip of the iliac crest around the posterior surface of the cecum, reaching medially to the level of the ureter so that the cecum can be mobilized and the posterior wall can be elevated and rotated anteriorly and medially.

Palpation of the posterior wall of the cecum now discloses the tumor of the inflamed appendix (Fig. 3). Turning the cecum anteromedially directing the posterior wall anteriorly and retracting outside the peritoneum (the overlying small bowel) access may now be had to the peritoneum overlying the diseased area (Fig. 3). The peritoneum is intact until this next step.

Fig. 1. Wide separation of external oblique aponeurosis from internal oblique.

Fig. 2. Digital retraction of internal oblique and transversus from peritoneum, the starting point for separation of the peritoneum posteriorly.

Fig. 3. Rotation of cecum anteriorly showing underlying tumor of the appendix. Allis forceps are on the exposed peritoneum.

Fig. 4. Peritoneum opened and appendix extruded.

Fig. 5. Removal of appendix.

Fig. 6. Showing type of appendix, hemorrhage into lumen, and localitis.

¹Sloan, LeRoy Hendrick. *Practice of Medicine*, Tick, Vol. VII, p. 491a. Hagerstown, Md.: W. F. Prior Co., Inc.



Fig 1



Fig 2



Fig 3



Fig 4



Fig 5



Fig 6

This peritoneum is now incised and the appendix is permitted to extrude itself. It can be gently aided if needed (Fig. 4). The presence of fecaliths with necrosis of the wall of the appendix in this position necessitates extreme care in handling at this point, as the appendix in this position is often friable (Fig. 5).

If an abscess cavity of limited area exists around the posterior cecal wall, the anterior margin of the peritoneum may be sutured to the posterolateral cecal wall or to the lateral cecal wall, exteriorizing from an abdominal point of view the infected area. If necrosis of the posterior wall of the cecum has occurred, it should be inverted by sutures. Into this area a Mikulicz drain is placed through a lumbar stab wound. The closure of this pento-

neum is otherwise without drainage, and the wound is closed in layers with sutures of catgut.

SUMMARY

Acute retrocecal appendicitis may be recognized clinically by a vertical line of tenderness extending upward from the iliac crest, 6 to 8 centimeters posterolateral to the anterior superior spine, to the tip of the appendix, often below the rib margin.

The clinical course is often slower in development than other types, due to the relative absence of peritonitis.

A surgical approach to this retrocecal appendix which has proved of advantage is described.

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THE TONUS OF THE UTERUS DURING PREGNANCY AND ITS RELATION TO LABOR

A Study of 1028 Observations Made With the Lóránd Tocograph

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OBSTETRICIANS have paid little attention to the hardness or tonus of the human uterus that is present between the intermittent contractions which occur during pregnancy. This has been due chiefly to the lack of a suitable means for measuring it. The development of the tocograph (1) however has supplied such a need. It has demonstrated that tonus varies from patient to patient at identical periods during pregnancy as well as in the same patient at different times.

It need hardly be mentioned that the character of labor varies likewise from patient to patient, and it is equally well known that we do not possess, at the present time, any means for predicting what the nature of the labor may be. These facts raised the question as to whether there might not be a significant correlation between the tonus of pregnancy and the character of the labor. If such were the case the information resulting from a consideration of the relationship would have definite practical value and if not a study of tonus would at least throw some light upon a little understood characteristic of uterine physiology.

In previous communications (2-3) we reported upon the variations in the tonus of the uterus which occur during pregnancy and labor. These observations were relatively few in number. Since they were published additional ones have been made, which include the recording of some unusually high degrees of tonus. These facts together with our desire to determine the exact relation between pregnancy tonus and the character of labor have led to the present re-examination of all of our available material.

MATERIALS AND METHODS

The observations were made between August, 1938 and April 1941 upon patients attending the Maternity Department of the Hospital of the University of Pennsylvania, and ones residing in a private maternity home in Philadelphia.

Measurements of tonus were secured with a Lóránd tocograph which has been described fully elsewhere (1). In brief however it is a mechanical kymograph which registers uterine movements through the medium of the abdominal wall.

Tonus is measured in the following manner. The clockwork of the tocograph is started, and the recording pen is allowed to draw a base line upon the recording paper before the machine is placed upon the patient. With the latter in the supine posture the tocograph is then placed upon the most prominent part of her abdomen.

If the uterus is relatively soft when the tocograph is placed upon the abdomen, the button projecting from the bottom of the machine buries itself full length in the abdominal wall, and thus the recording pen connected with the button fails to be dislodged from its base line position. Under these conditions, the patient is classified as exhibiting no increase in tonus (Fig. 1 226). Above a certain yet unknown, degree of uterine tonus, the tocograph button meets sufficient resistance in the abdominal wall to displace it into the machine, thus dislodging the recording pen from its base line position. Under these conditions, the patient is classified as exhibiting an increase in tonus (Fig. 1 227). The amount of the latter is estimated in terms of the distance traversed by the pen under extreme circumstances this may reach a maximum of 25 millimeters. For a more detailed consideration of the condition represented by the term tonus, the reader is

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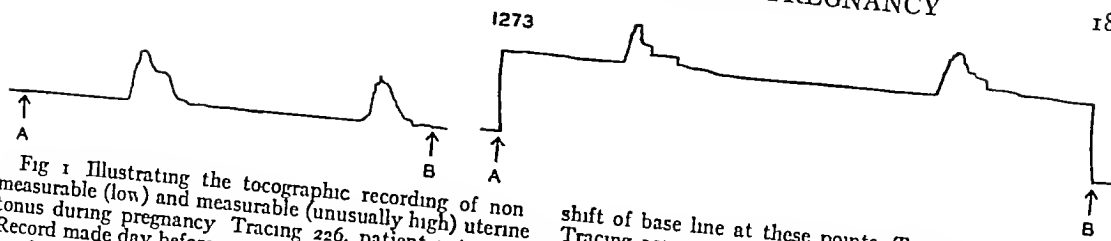


Fig 1 Illustrating the tocographic recording of non-measurable (low) and measurable (unusually high) uterine tonus during pregnancy Tracing 226, patient a tripara Record made day before onset of labor Tocograph placed on abdomen at A and removed at B Note absence of any

shift of base line at these points Tonus nonmeasurable Tracing 1273, patient a tripara Record made day before onset of labor Tocograph placed on abdomen at A and removed at B Note elevation of base line between these two points Tonus measurable and quite high (13 mm)

referred to the evaluation which appears at the end of this report

RESULTS

A group of 435 patients supplied a total of 1,028 tocographic records These were secured from the 79th day of pregnancy to the day before labor, inclusive The number of records per individual appears in Table I The observations are presented under two headings (1) "Tonus in Relation to Pregnancy," and (2) "Tonus in Relation to Labor"

Tonus in relation to pregnancy In a selected group of individuals recordings were made at regular intervals Table II shows the incidence of tonus and its degree in 15 patients who were observed at weekly intervals throughout the 9 or more weeks immediately preceding labor A measurable increase in tonus occurred rarely before the 33rd week of gestation, even after that time, both the incidence and degree varied widely Patient 14 registered no increase at any time before the onset of labor In contrast to her, patient 6 exhibited measurable tonus as early as the 30th week, and practically every week thereafter Patient 4 showed no tonus until the last week of gestation

The presence of measurable tonus at any one time was no indication that it would be found at the time of subsequent recordings, though such was more likely to be the case These data emphasize the variability with which a measurable increase in tonus appears in the same person from week to week, and in different persons at the same period of gestation

In an unselected group of individuals recordings were made at irregular intervals (Tables III, IV, and V)

The influence of advancing pregnancy upon the incidence of a measurable increase in tonus is given in Table III which lists the percentage of tocographic tracings registering a measurable amount of tonus, arranged according to gravidity and to the time in pregnancy that they were secured This degree of tonus was observed in primigravidas as early as the 6th lunar month of pregnancy, but not until the 7th month in the case of multigravidas Primigravidas exhibited their first significant increase in the incidence of measurable tonus, during the 8th month, whereas multigravidas did not do so until one month later During the 10th lunar month, 58.6 per cent of tracings of primigravidas showed an increase in tonus, in contrast to 37.9 per cent of observations upon multigravidas Thus, only 48.4 per cent of tracings of primigravidas and multigravidas combined, recorded a measurable increase in tonus during even the last month of gestation

The influence of advancing pregnancy upon the degree of increase in tonus is recorded in Table IV which shows the average and maximum amount of tonus observed in the tracings of those patients who exhibited a measurable increase in tonus The degree of tonus increased progressively as pregnancy ad-

TABLE I — TOCOGRAPHIC RECORDS PER INDIVIDUAL

Tocographic records	Individuals
1	272
2	74
3	29
4	18
5	6
6-10	18
11-15	11
16-20	4
21-25	3
Total	435

TABLE II.—INFLUENCE OF PREGNANCY UPON UTERINE TONUS

Duration of gestation in weeks	Uterine tonus									
	Patient identification									
				5	6	10	13	17	21	
16										
17										
18										
19										
20										
21										
22										
23										
24										
25										
26										
27										
28										
29										
30										
31										
32										
33										
34										
35										
36										
37										
38										
39										
40										

Table II. Showing influence of advancing pregnancy upon incidence and degree of measurable tonus in 5 patients who are studied at weekly intervals for the 9 or more weeks immediately preceding labor. O indicates absence of measurable tonus. Other numerals represent measurable tonus expressed in millimeters. NT stands for no tracing. Note () Definite increase in the number of tracings showing measurable tonus after the 30th week of pregnancy; (b) variability both in occurrence and in degree of tonus in some patient from week to week, and in different individuals at the same period of pregnancy; (c) generally increased tonus during the 40th week, although some patients exhibited no measurable tonus at this time.

vanced. By the end of pregnancy however the amount of tonus was practically identical in primigravidae and multigravidae.

The influence of the last 14 days of pregnancy upon uterine tonus is shown in Table V which

TABLE III.—INFLUENCE OF ADVANCING PREGNANCY UPON UTERINE TONUS

Lower month of pregnancy	Tocographic records of									
	Primigravidae and multiparavidae					Primigravidae		Multigravidae		
	Records	Showing increase in tonus				Records	Showing increase in tonus	Records	Showing increase in tonus	
		No.	%				No.	%		
3rd										
4th										
5th	13									
6th	11					10	11	1	1	
7th	87					36	6	19		
8th	11	11	11.1			11	11	11		
9th	190	61	31.1			49	29.5	66	31	31.1
10th	847	113	13.4			193	22.6	279	27.1	

Table III. Showing the influence of advancing pregnancy upon the frequency with which measurable tonus was observed in 1,038 tocographic tracings, arranged according to gravidity. Note () Absence of measurable tonus prior to the 6th lower month in the case of primigravidae, and prior to the 7th month in multigravidae; (b) progressive increase in incidence of measurable tonus as pregnancy advances; (c) absence of measurable tonus during the last month of pregnancy in more than half of the tracings; (d) greater frequency of measurable increase in tonus throughout pregnancy in primigravidae than in multigravidae.

TABLE IV.—INFLUENCE OF ADVANCING PREGNANCY UPON UTERINE TONUS

Lower month of pregnancy	Records showing an increase in tonus					
	Primigravidae			Multigravidae		
	Records	Average	Maximum	Records	Average	Maximum
6th	1					
7th	1.0					
8th		± 0.4	1.0			
9th	49	1		149.5	1	
10th	191	1	0.5	11	1.1 ± 1.4	1
Total	241			161		

Table IV. Showing the influence of advancing pregnancy upon the degree of tonus observed in 249 tocographic records which registered measurable increase. Note (a) Progressive increase in the degree of tonus as pregnancy advances; (b) absence of any significant effect of gravidity upon degree of tonus even during the last month of pregnancy.

TABLE V—INFLUENCE OF LAST 14 DAYS OF PREGNANCY UPON UTERINE TONUS

Days before labor	Primigravidas and multigravidas			Primigravidas			Multigravidas		
	Total records	Tonus increased		Total records	Tonus increased		Total records	Tonus increased	
		Records	Average increase		Records	Average increase		Records	Average increase
14	16	8	mm 2.9	7	4	mm 3.9	9	4	mm 1.8
13	25	9	2.2	16	8	2.3	9	1	1.0
12	17	8	3.4	6	4	3.7	11	4	3.0
11	21	8	4.4	14	6	5.3	7	2	1.5
10	23	5	3.8	15	3	4.3	8	2	3.0
9	27	12	4.8	13	7	3.6	14	5	6.5
8	32	17	3.0	13	8	2.7	10	9	3.2
7	24	13	3.9	13	10	3.6	11	3	5.1
6	32	15	5.8	14	8	4.9	18	7	6.9
5	30	19	3.8	9	7	3.3	21	12	4.1
4	28	15	5.4	16	13	5.7	12	2	3.4
3	26	12	2.8	15	8	3.0	11	4	2.5
2	50	34	5.0	25	22	5.6	25	12	3.8
1	100	60	5.2	44	32	4.9	56	28	5.6

Table V Showing the influence of the last 14 days of pregnancy upon the incidence and degree of measurable tonus as observed in 451 tocographic tracings. Note (a) Relatively constant occurrence of measurable tonus, (b)

the slight but gradual increase in degree of tonus, (c) the absence of any abrupt change in tonus, (d) the absence of any effect of gravidity upon either characteristic

gives (a) the number of tocographic tracings made during the last 14 days of pregnancy, (b) the number of these which registered a measurable increase in tonus, and (c) the average increase in the latter group. The data in this table indicate (a) the marked variability in the incidence of measurable tonus at this time and also (b) the similar variability in the degree of increase. Furthermore, they show that no sudden change in either characteristic takes place at this time, although there was a tendency for the tonus to become stabilized during the few days immediately preceding labor.

Tonus in relation to labor. Table VI shows the influence of tonus, registered during the last 4 weeks of pregnancy, upon the duration of labor of primigravidas. Each record represented a different patient, no individual exhibited any evidence of cephalopelvic disproportion, all deliveries were vaginal, the infants had cephalic presentations and weighed between 2,500 and 3,500 grams at birth.

The data in the two left-hand columns of Table VI were supplied by patients exhibiting no measurable increase in tonus. Patients who registered a measurable increase supplied the information in the right-hand columns.

The average duration of labor of the patients whose tonus was above the average of those who exhibited measurable tonus did not differ significantly from that of the patients who recorded no measurable tonus at the same periods of pregnancy, respectively.

Table VII shows the influence of tonus, upon the duration of labor of multigravidas. As in the case of primigravidas, the amount of tonus present during late pregnancy had no influence upon the duration of labor.

As to the influence of an unusually high tonus during the last week of pregnancy upon the duration of labor the following is recorded. Eight primigravidas experienced an unusually high degree of tonus (10 to 17 millimeters). One (tonus 15 millimeters) gave birth to a 4,500 gram infant by forceps after a prolonged

TABLE VI.—INFLUENCE OF TONUS
UPON DURATION OF LABOR

Primigravidas

Week of pregnancy	Tonus			
	Not measurable		Above average	
	Number of records	Average duration of labor	Number of records	Average duration of labor
27th	10	Hours 14		Hours 12
28th	10	14.5		12
29th	14	14.4	8	8
30th	13		15	6.2
W. A.		14.3		5

Table VI. Showing the average duration of labor of group of primigravidas from whom tocographic records were secured during the last 4 weeks of pregnancy arranged according to whether measurable tonus was absent, or above the average in the group that exhibited measurable tonus. Note that the average duration of labor was slightly shorter in the group which exhibited tonus above the average. Compare with data in Table VII.

TABLE VII.—INFLUENCE OF TONUS
UPON DURATION OF LABOR

Multigravidas

Week of pregnancy	Tonus			
	Not measurable		Above average	
	Number of records	Average duration of labor	Number of records	Average duration of labor
27th	13	Hours 7	3	Hours
28th	20	8.5		
29th	27	8		11
30th	17	8	17	7
W. A.		8		

Table VII. Showing the average duration of labor of group of multigravidas from whom tocographic records were secured during the last 4 weeks of pregnancy arranged according to whether measurable tonus was absent or above the average in the group that exhibited measurable tonus. Note that the average duration of labor was shorter in the group which recorded no measurable tonus. Compare with data in Table VI.

second stage. Another with a tonus of 17 millimeters was delivered by cesarean section on account of cephalopelvic disproportion and primary inertia. A third patient had a breech delivery. The 5 remaining delivered spontaneously only 1 having a slightly prolonged second stage.

Five multigravidas also registered an unusually high degree of tonus (10 to 13 millimeters) during the last week of pregnancy. The labors of all were short, no second stage lasted longer than 45 minutes, 3 of the deliveries were precipitous.

There was no evidence to indicate that the high tonus of any patient influenced adversely the course of labor. If it had any appreciable effect whatever it aided rather than retarded delivery.

EVALUATION OF STUDY

The present observations indicate that, within certain limits, tonus can be measured with a satisfactory degree of accuracy during pregnancy. This statement is based upon (a) repeated observations upon the same individual at intervals of hours, days, weeks and months and (b) by comparing repeated ob-

servations upon one individual with those of another. Uniform results have been secured from individuals who varied considerably both in weight and in the thickness of their abdominal walls. In carrying out the measurement the tocograph usually is placed in the midline and above the umbilicus, where the abdominal wall is relatively thin and in close contact with the upper pole of the uterus. Furthermore, the registering of the tonus is not influenced by the tightness of the belt which holds the tocograph in position, since varying this factor has no influence upon the measurement.

Although the method of measurement is satisfactory it is not fully established as to just what is being measured. Wolf who has compared measurements made with intra-uterine bags with those secured by external hysterography concludes that the latter records the hardness of the uterine wall rather than intramterine pressure. The present author concurs in this belief. Whichever characterizes the measurement represents, it is certainly only relative, but nevertheless useful as a means for comparing one patient with another.

It is apparent that tonus varies considerably during pregnancy, but no evidence is forthcoming as yet to explain why these variations occur

It is an interesting observation that a measurable increase in tonus occurs earlier in primigravidas than in multigravidas, and that more of the former experience it throughout pregnancy than do the latter. On the other hand, the degree of tonus attained at the end of pregnancy appears to be the same in primigravidas as in multigravidas. One might expect it to be higher in primigravidas at this time, in view of the fact that it appears earlier and more often in them than it does in the multigravidas.

There appears to be an unusual increase in the incidence of measurable tonus during the 8th lunar month of pregnancy, but no significant change in it during the 2 weeks immediately preceding the onset of labor. It follows from this that knowledge of the degree of tonus present just before labor is of no aid in predicting the time of onset of labor. Nor has any evidence come to light to indicate that a study of tonus alone is of any value in predicting the quality of the uterine activity at the time of labor.

The methods employed in securing the present data have their obvious limitations. These include the fact that the tocograph has the inherent weakness of any precision instrument operated by a spring, that the present observations were made by several different individuals, who employed a number of different tocographs. It is believed, however, that some of the difficulties encountered are outweighed by the number of observations made.

SUMMARY AND CONCLUSIONS

1 A series of 435 patients supplied 1,028 tocographic records of what, for want of a better term, may be described as uterine tonus during pregnancy.

2 Detectable increases in tonus were observed first in primigravidas during the 6th lunar month, and not until the 7th month in the case of multigravidas.

3 Wide variations in tonus were observed in the same patient at different times during pregnancy and in different individuals at similar periods of gestation.

4 Tonus increased progressively in degree as pregnancy advanced, in those patients who exhibited a measurable amount.

5 An unusual increase in tonus appeared in primigravidas during the 8th month, but not until the 9th month in the case of multigravidas.

6 Although primigravidas experienced increases in tonus earlier and more often in pregnancy than did multigravidas, the ultimate level of their tonus did not exceed that of the multigravidas.

7 During the last lunar month of pregnancy, less than half of all patients exhibited any measurable tonus.

8 From these observations, it is concluded that knowledge of the uterine tonus present during pregnancy is of no value in predicting either the time of onset of labor or its character.

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THE FUNCTIONAL ANATOMY OF LABOR AS REVEALED BY FROZEN SAGITTAL SECTIONS IN THE MACACUS RHEBUS MONKEY

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UNTIL recently our concepts concerning the action of the human uterus were based almost wholly upon principles which were developed nearly half a century ago. These principles arose from two general sources: first, clinical observation of the laboring uterus, and second, studies of frozen sagittal sections of women who had died in labor. A relatively large number of human frozen sections have been made and their study has contributed much to our knowledge. However the sections have been made under such varying circumstances, in regard to the cause of death and the type of labor as to engender skepticism concerning their true representation of the normal process. The freezing methods were slow and in some instances the specimens were not frozen until a number of days after death.

Since the evidence obtained by the frozen section technique is essential for a thorough understanding of the process of evacuation of the uterus, our work was undertaken to obtain such evidence under uniform conditions as to the cause of death and the time and method of freezing. It was believed that the possession of such evidence for the uterus of a subhuman primate would supplement and render it possible to evaluate more accurately the evidence supplied by the human specimens.

In this study rather extensive chronological evidence of the anatomicophysiological changes occurring in the laboring monkey uterus has been obtained. The *Macacus rhesus* was chosen as a suitable subject because of our familiarity with the uterus of this animal, because of its close anatomical and physiologi-

cal similarity to the human uterus, and because certain points of evidence required could never be obtained in the human being. Of course, results obtained in one species must be applied to another with reservation. However our knowledge of the gross, comparative, and functional anatomy of the rhesus uterus indicates that the processes concerned in evacuation should be fundamentally the same in both species.

ANATOMICAL CONSIDERATIONS

Before considering our own data, it is important to obtain a clear understanding of the anatomical divisions of the nonpregnant uterus and their fate in early pregnancy. These points are stressed, first, because they are essential to an adequate understanding of the subject which we wish to present, and, second, because they are not generally used despite their thorough and adequate demonstration.

Until the early part of the present century the human uterus was considered as being composed of two essential parts: cervix and corpus. The term "isthmus" had been employed upon occasion, but it was not until the work of Aschoff in 1905 that the isthmus was seen to be a definite structure, distinct from both cervix and corpus, anatomically as well as functionally. Since this time the subject has been considered by numerous authors, the overwhelming majority of whom subscribe to Aschoff's observations. The work of Stieve, in 1927, has emphasized and extended the observations of Aschoff and now serves as the classic description of cervix and isthmus uteri and their intrinsic changes in pregnancy, labor, and the puerperium. In addition to these, the comprehensive article by Frankl is most valuable.

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This work was made possible by a gift in honor of Dr. I. M.
Danforth.

The uterus is now considered as being composed of 3 essential parts the cervix, isthmus, and corpus. The cervix and corpus require no description in this communication.

When the uterine cavity is examined in a frontally sectioned uterus, the cavum corporis is seen to terminate inferiorly by a narrow canal, which soon widens into the spindle-shaped canal of the cervix proper. The length and structure of this canal varies in different specimens, and with parity. Ordinarily it is approximately 6 to 10 millimeters in length, and slightly narrower at its superior extremity. In many specimens the lower extremity can be distinguished grossly, but in others the canal terminates gradually in the cervical lumen. It is to the tissue which surrounds this canal, throughout the thickness of the uterus, that the term *isthmus* has been applied. The "anatomical internal os," is discernible with the naked eye. It is a definite muscular constriction which is often referred to, inadequately, simply as the "internal os." Aschoff adds that "at this point, where there is distinguishable externally a slight constriction, where as a rule there is the tight adhesion of the peritoneum, and where the first large transverse branches of the uterine artery enter the muscle substance, lies the upper limit of the isthmus." Again, to quote Aschoff, the lowermost extent of the isthmus is the so called "*histological internal os*," is the "line of demarcation between the (columnar) epithelium of the cervical canal and the corporeal epithelium, but not, as is so often said, the upper limit of the arbor vitae. The fold formation cannot be used in the determination of the line of demarcation. Furthermore, here the cervical and corporeal glands mingle." The transition from cervix to isthmus is therefore a gradual one, which occurs over the course of 1 or 2 millimeters. Frankl states that with experience this transition is often distinguishable grossly. Structurally, the isthmus resembles the corpus, but there are certain essential differences. The mucosa is thinner than that of the corpus, is richer in supporting tissue, and poorer in glands. The musculature is more poorly developed than that of the corpus, better so than that of the cervix.

The following changes are reported during pregnancy. Until the end of the second month the canal of the isthmus remains narrow, but it lengthens considerably, up to 2 to 3 times its former length. (It is of incidental interest that when a vaginal hysterotomy is performed at this stage of pregnancy one might, unless cognizant of these isthmic changes, attribute the greatly increased distance from external os to ovum chamber as being due solely to an increase in the length of the cervix. Stieve's investigations show quite clearly that there is no significant increase in cervical length. The increased distance from anatomical internal os to external os is due almost entirely to lengthening of the isthmus.) In the third month the wall of the isthmus unfolds quite rapidly, and the canal widens to form a part of the general uterine cavity. From this time until the conclusion of pregnancy, the boundary between the general uterine cavity and the cervical canal is the histological internal os of Aschoff, which now becomes known clinically as the *obstetric internal os* (O I O). (This differentiation is important, since it emphasizes the inadequacy of the unqualified term "internal os.") At term the isthmus uteri measures from 7 to 10 centimeters in length, thus making up between one fifth and one fourth of the total sagittal length of the uterus.

The nonpregnant monkey uterus. Three nonpregnant rhesus uteri have been studied. A section of one of these is shown in Figure 1. The major difference between the rhesus and human uterus is the cervical canal, which is straight in the latter, tortuous in the former. The tortuosity of the rhesus cervical canal is due to the presence of nipple-like projections (colliculi) from the walls of the cervix. Our findings concerning the location of these colliculi are not entirely in agreement with those reported by other workers and will be considered in detail in a later communication. Briefly, in all of the specimens studied we have observed 4 such projections, the 2 upper lips of the cervix, the 2 lowermost, the external cervical lips. Histological examination of the nonpregnant specimens indicates that the cervical canal extends from the ex-

ternal cervical lips to a point on the upper aspect of the internal lips. The isthmus appears to extend from this latter point upward for a distance of 8 to 10 millimeters. The remainder is corpus.

It is of interest that a physiological sphincter exists in the rhesus uterus at the junction of cervix and isthmus (at the site of the obstetric internal os). This can be felt to contract about the examining finger and balloon records can be made of its activity (Ivy Hartman and Koff Danforth and Ivy).

Changes in the monkey uterus during pregnancy. No sections during early pregnancy are included in our series of animals. The work of Franke upon an allied species (*Cercopithecus cynomorpha*) however serves to fill this gap. Despite the fact that his work was done before the demonstration of the isthmus uteri Franke's careful descriptions leave little doubt of the fate of this structure during early pregnancy. According to his observations, the isthmus in this species unfolds and the canal widens in a manner which is essentially similar to that described for the human being. After the widening occurs, the junction between the uterine cavity and the cervix is at the level of the internal lips of the cervix. This latter is in agreement with our findings. Thus the internal lips definitely mark the obstetric internal os anatomically so that it may be followed throughout labor.

METHODS

Thirty three *Macacus rhesus* monkeys were studied. Three were nonpregnant controls. Three were sacrificed late in pregnancy prior to the onset of labor. Six were sacrificed at various stages from the onset of labor to complete effacement and dilation of the cervix. Sixteen were sacrificed during the second stage of labor: 1 during the third stage, and 4 at various intervals from hour to week post partum.

The descriptions by Hartman and by Hartman and Straus were found to be most helpful in the diagnosis of labor in the early animals of this series, and in the handling and care of all the animals.

The progress of labor was followed by abdominal palpation and digital vaginal examination. When the desired stage of labor was reached the animal was lightly anesthetized with intravenous sodium pentobarbital. This drug did not inhibit the uterine contractions perceptibly. The anesthetized animal was fastened by light cords to a rectangular metal frame which maintained a modified lithotomy posi-

tion. At the height of a uterine contraction the animal was lowered into the freezing chamber.

The freezing solution was kept ready for immediate use. The chamber consisted of an insulated, galvanized iron tank containing a mixture of 95 per cent ethyl alcohol and chipped dry ice (solid carbon dioxide). After a period of time this mixture reaches a temperature of -70 to -80 degrees $C.$, and maintains itself there until all the dry ice has vaporized.

While freezing, the animals were kept completely submerged. They were allowed to remain in the chamber for at least one hour so that they reached the temperature of the freezing mixture.

By means of a motor driven band saw, with a movable platform, the upper abdomen, tail and lower legs were removed, and a median sagittal section of the remaining torso was made. The cervix was cleanly bisected in all instances.

While in the frozen state direct outline tracings of the sections are made and measurements taken, both the specimens themselves and the tracings being utilized. Precise pen and ink drawings were prepared by the artist from the direct tracings. Wash drawings are prepared from the specimens in order to illustrate certain points of detail which were not apparent in the pen and ink. In each of the frozen specimens, a section was made one half inch lateral to the midline. This half inch slice was placed in 1 per cent formalin, and from it histological sections of the uterus were made. These are not reported here, except in so far as they are necessary for the confirmation of results.

Of the 33 specimens available, 21 representative ones have been selected for reproduction at this time.

In regard to the measurements, it is emphasized that it is our purpose not to present a rigid statistical analysis of labor but rather to gain knowledge of the general trends in labor. The variation in measurements of this type is considerable, and the possible ways of measuring the same structure are legion. In order that variations might be reduced to a minimum, all measurements were made by the same individual utilizing precisely the same technique in all specimens. All measurements were verified at least twice. It is perhaps unnecessary to point out that rigid statistical treatment of results such as these is a meaningless procedure.

The following measurements and ratios are presented at this time:

1. The total internal sagittal circumference of the uterus.
2. The greatest length from the internal aspect of fundus to plane of external os.

TABLE I—EXAMPLE OF COMPLETE LABOR
PROTOCOL, MONKEY NO 14 (SERIES NO 8)
DATE MAY 19, 1938

TABLE II—SHOWING (1) THE RELATION OF THE
TOTAL INTERNAL CIRCUMFERENCE (A) TO
THE LENGTH FROM THE INNER ASPECT OF
THE FUNDUS TO THE PLANE OF THE EX-
TERNAL OS (B), AND (2) THE RELATION OF
INTERNAL CIRCUMFERENCE FROM OIO
TO OIO (C), TO THE LENGTH FROM IN-
TERNAL FUNDUS TO PLANE OF OIO (D) *

Time	Remarks
7 15 p m	Animal lay down, appeared somewhat more nervous than usual Her face was flushed in a manner similar to that of previously observed laboring monkeys
7 25 p m	Vaginal examination Cervical dilatation 1 5 cm Contractions of fairly good quality, occurring every 2 to 2 1/2 minutes, lasting 30 to 35 seconds Forewaters bulging through cervix with each pain
7 30 p m	Animal tied down to allow precise observation
8 45 p m	Vaginal examination Findings essentially the same as noted above
8 50 p m	Animal allowed up in cage
9 00 p m	More restless with pains
9 10 p m	Vaginal examination Cervix partially effaced, dilated 2 cm Pains of good quality, occurring every 2 to 2 1/2 minutes and lasting 35 to 40 seconds
9 25 p m	Vaginal examination Cervix fairly well effaced, dilated 2 to 2 5 cm Head entering the pelvis
9 30 p m	Anesthetized
9 35 p m	Freezing started Temperature of the bath -72 degrees C
10 35 p m	Animal removed from freezing mixture

Stage	Total circumference E O to F O A	Great est length fundus to plane of E O B	Ratio B-A	Total circumference OIO to OIO with lips C	Great est length fundus to plane of OIO with lips D	Ratio D+C
Before labor (term?) (Cases 1-3)	36 4	14 5	40 0	35 0	14 4	41 1
I (Cases 5-9)	43 3	17 4	40 1	41 0	16 1	40 0
II A (Cases 10-12)	34 9	14 4	41 5	31 7	12 9	40 7
II B (Cases 13-19)	30 1	12 3	40 8	27 4	11 0	40 1
II C (Cases 20-25)	26 1	11 0	42 1	22 5	8 6	38 2
III	18 5	7 2	39 0	17 3	6 8	39 3
P P—1 hour to 3 days	18 1	7 6	40 3	15 3	6 2	43 8
P P—1 week	15 0	6 7	44 6	12 9	5 8	44 9
Nonpregnant	9 1	4 4	48 3	6 7	3 2	47 7

OIO obstetric internal os E O external os
*Since the internal circumference is obviously irregular the extent of the accuracy of the measurements may be subject to question. This problem can be tested by ascertaining whether the circumference bears a rather constant ratio to the length or long diameter of the uterus which is roughly an ellipsoid. The ratios are surprisingly constant, and prove the relative accuracy of the method of measurement. Measurements in this table as in others are in centimeters

3 Relation of the cervical lips to the anatomical conjugate, to the symphysis, and to the promontory of the sacrum (In this report the term true conjugate is used synonymously with anatomical conjugate, to indicate the distance from the superior edge of the symphysis to the sacral promontory. It is to be distinguished from the obstetrical conjugate which is the shortest distance from the symphysis to the promontory)

4 Sagittal circumference of the uterine cavity from obstetrical internal os anteriorly to obstetrical internal os posteriorly

5 Total length of the cervix

6 Sagittal circumference of the uterus below the insertion of the placenta, or below a retraction or constriction ring

For purposes of comparison all of the published human frozen sagittal sections were subjected to similar, though necessarily less exact, measurement. These are not included in the present report, except to indicate certain points of similarity

RESULTS

In the discussion of results, the first and third stages of labor have been considered in accordance with the usual definitions, respec-

tively, from the onset of labor until complete dilatation of the cervix, and from delivery of the babe until after the birth of the placenta. For purposes of description it has been found advisable to divide the second stage into 3 sub-stages, rather than to consider it as a whole as is customary. Substage II A has been used to designate the changes occurring from the time of complete dilatation until separation of the lower border of the placenta occurs (v1). Substage II B has been used to indicate the changes occurring from the time of separation of the lower border of the placenta up to, but not including, the birth of a part. Substage II C includes the changes from the birth of a part to the birth of the entire fetus. These sub-stages are clearly evident in our sections. An example of a complete labor protocol is shown in Table I

TABLE III.—THE RELATION OF THE CERVICAL LIPS TO THE ANATOMICAL CONJUGATE, TO THE LEVEL OF THE SYMPHYSIS, AND TO THE LEVEL OF THE PROMONTORY

Stage	Lips as related to anatomical conjugate				Lips as related to symphysis				Posterior lips as related to anal promontory	
	Anterior		Posterior		Anterior		Posterior			
	External	Internal	External	Internal	External	Internal	External	Internal		
Before labor (term?)	—	—	— 3	—	— 0	+ 0 6	+ 0	+	External	Internal
I	—	—	—	— 8	— 0 6	— 0	+	+		— 4
II A	+ 4	+ 6	—	+ 0	+	+ 6	+	+ 3	6	+ 4
II B	+ 3	+	— 0	+	+	+	+	+	— 0	+
II C	+	+	— 0	+	+	+	+ 6	+		— 0
III	—	—	— 0	+ 0	— 0	— 0	+	+		— 0
P P hour to 3 days	—	—	— 2	—	— 0	+ 0 3	— 4	+ 6	— 7 0	— 2

— Centimeters below structure in question
+ Centimeters above structure in question

Of the 30 specimens during labor illustrations of 10 have been selected for reproduction at this time, as representative of the changes which have been observed. These are the following

1 (Monkey 4, Series 6) Questionable early labor. Dilatation 1 cm. by vaginal examination. (Figs. 4 and 5a.)

2. (Monkey 14, Series 8) See Table I. (Figs. 3 and 3a.)

3. (Monkey 19, Series 9) In labor 1 hour and 45 minutes. Dilatation 4 cm. by vaginal examination. Forewaters protruding through external os. (Figs. 4 and 4a.)

4. (Monkey 30, Series 1) Duration of labor unknown. First vaginal examination revealed complete dilatation. Sacrificed immediately (Figs. 5 and 5a.)

5. (Monkey 30, Series 6) In labor about 1 hour. Head upon the perineum. (Figs. 6 and 6a.)

6. (Monkey 10, Series 19) In labor 1 hour and 5 minutes. Bearing down with pains for about 25 minutes. Felt the vaginal introitus. (Figs. 7 and 7a.)

7. (Monkey 23, Series 20) Duration of labor unknown. Animal suddenly seen to be bearing down. After a period of observation, she was sacrificed immediately after delivery of the head. (Figs. 8 and 8a.)

8. (Monkey 30, Series 3) In labor 4 hours and 5 minutes. Sacrificed after delivery of head and thorax (Figs. 9 and 9a.)

9. (Monkey 32, Series 26) Sacrificed immediately after delivery of stillborn baby after labor of unknown duration. Placenta *in situ*. (Figs. 1 and 1a.)

10. (Monkey 30, Series 7) Precipitate labor. Sacrificed 1 hour after delivery of placenta. (Figs. 1 and 1a.)

The figures presented in Tables II to VII are averages for all specimens in the par-

TABLE IV.—REDUCTION OF THE INTERNAL CIRCUMFERENCE OF THE UTERUS WITH THE PROGRESS OF LABOR

Stage of labor	No. of cases	Circumference cm. O to O 10 with lips	Reduction (cm.) C	% Reduction C-A	Circumference cm. O to O 10 with-out lips A-B	Reduction (cm.)	% Reduction	Total length of both internal lips B
Before labor (term?)		39			32 6			
I		24			26			
II A (up to separation of placenta)		23		22	20	6	22	
II B (from some separation to birth of part)		27	12 6	23	16		23	
II C (after birth of part)	6	22	25	43	21	17	42	
III (placenta <i>in situ</i>)			23	53	14	54		
P hour to 3 days				62	22	25	66	
P P week		9	28	66 7	9	27	69	

ticular group indicated. All measurements were made from the sagittal surface only. It is regretted that lack of space prevents the publication of all of the measurements at this time, and that only averages of the entire stages may be presented. Trends which are apparent within the stages are thus not evident, except for those which are illustrated in the graph which is included. Certain of these trends will be mentioned, then, without presentation at this time of the evidence which substantiates them. Also, in order to conserve space, the ranges of the figures used in computation of the averages are not included in this communication. The figures are sufficiently constant that the authors ascribe definite trend significance to them.

ANALYSIS OF STUDY

The problem of precise differentiation of the fate of the various uterine segments in frozen sections of the human uterus offers difficulty because of the absence of gross fixed landmarks in this species. After dilatation of the cervix has started there is no definite means of

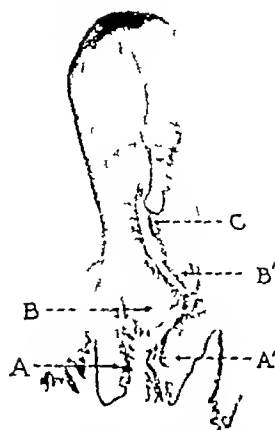


Fig. 1. Sagittal section of adult nonpregnant rhesus uterus, (11) A, A', external cervical lips, B, B', internal cervical lips, C, upper boundary of isthmus uteri

determining the upper boundary of the cervix. The bladder reflection, commonly stated as being a rather definite indication of the upper limit of the isthmus, has been found to be of no value in the instance of the human frozen sections. Similarly, this point has been most disappointing as a landmark in the monkey

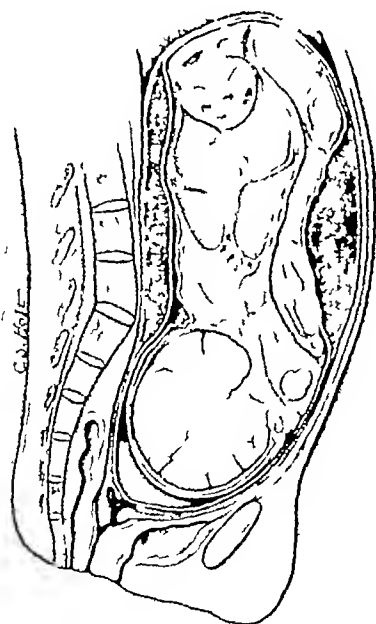


Fig. 2

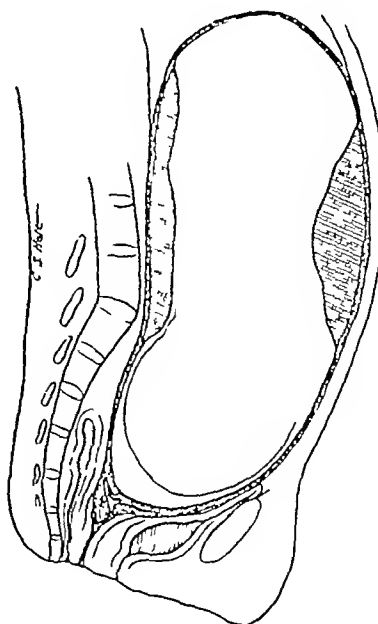


Fig. 2a.

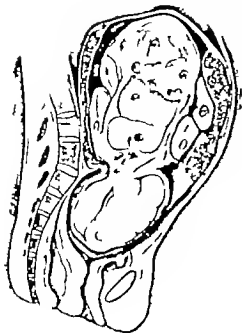


Fig. 4.

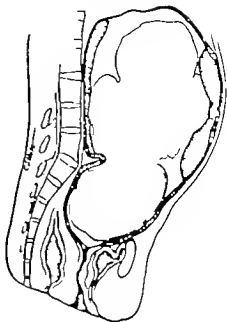


Fig. 32.

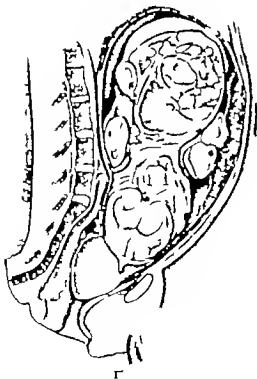


Fig. 33.

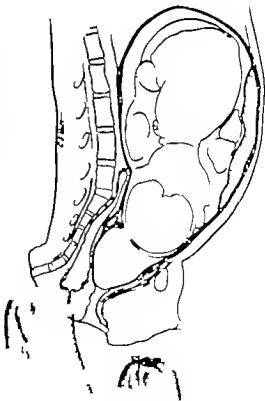


Fig. 34.

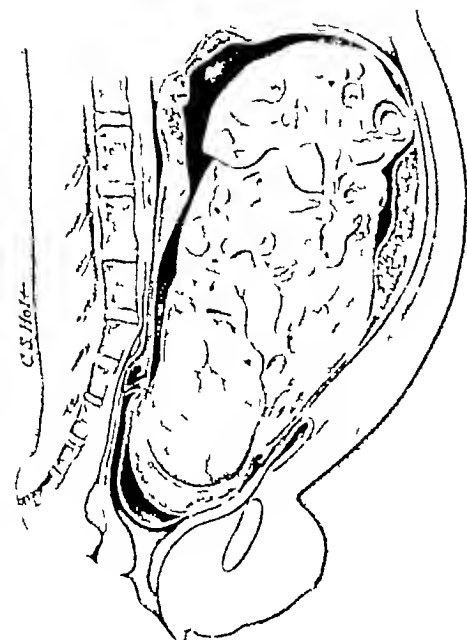


Fig 5

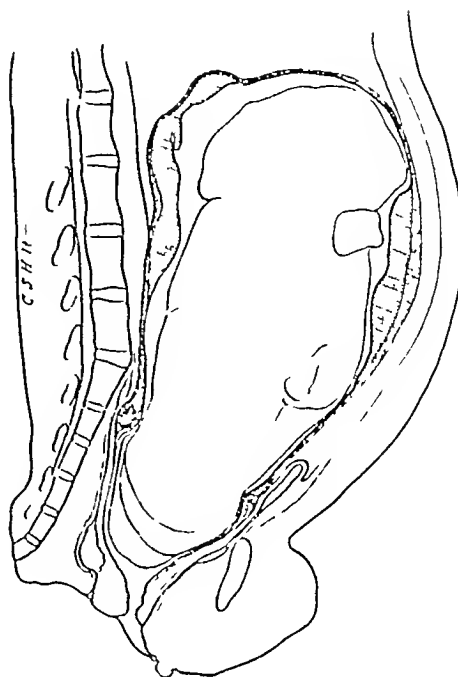


Fig 5a

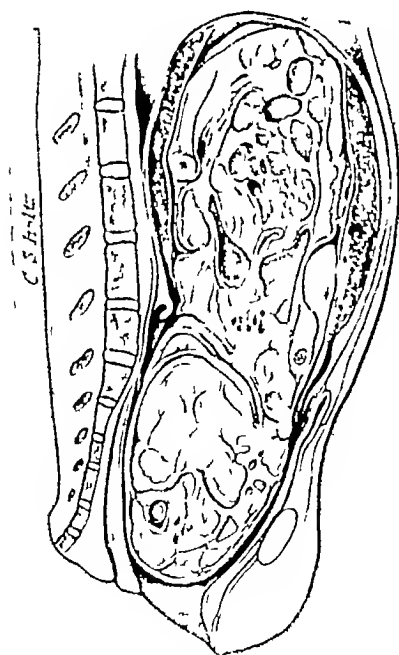


Fig 6

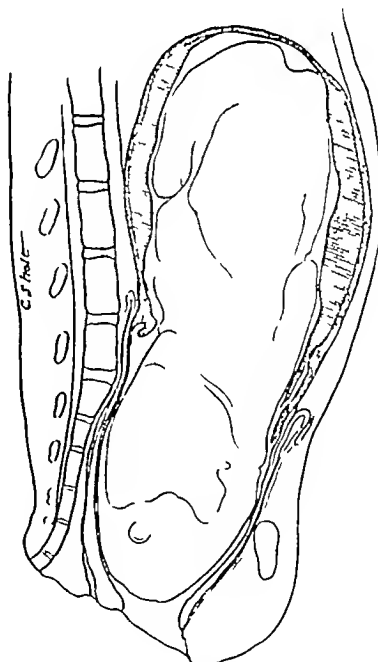


Fig 6a

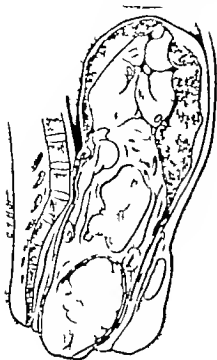


Fig. 7

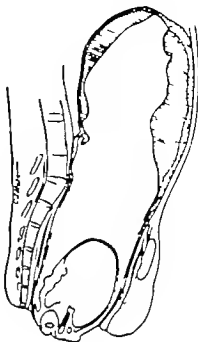


Fig. 7a

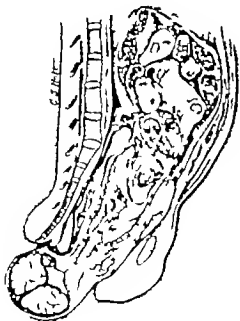


Fig. 8

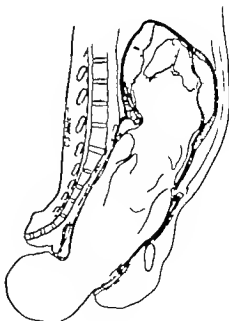


Fig. 8a

TABLE VI—THE PER CENT RETRACTION OF THE UPPER AND LOWER UTERINE SEGMENTS IN RELATION TO THE ORIGINAL INTERNAL CIRCUMFERENCE OF THE UTERUS AND TO THE ORIGINAL LENGTH OF THE SEGMENT IN QUESTION (FROM 0.10 TO 0.10)

Stage	No of cases	Circumference cm OIO to OIO with lips A	Circumference placenta to OIO (LUS) B	Circumference UUS (A-B) C	% of internal circumference made up by LUS	% of internal circumference made up by UUS	% retraction LUS	% retraction UUS	% decrease in circumference due to retraction of	
									LUS	UUS
Before labor (term?)	3	35 0	10 7	24 3	30 6	69 4				
I	5	41 0	13 0	28 0	31 7	68 3				
II A	3	31 7	6 7	25 0	21 1	78 9	†48 4	†10 7	67 7	32 3
II B	7	27 4	5 2	22	19 0	81 0	60 0	1 0	57 0	43 0
II C	6	22 5	5 6*	16 9	24 9	75 1	57 0	40 0	40 0	60 0

LUS, lower uterine segment or isthmic segment, UUS, upper uterine segment or 'corporeal segment.'

*This increase is due to the failure of the LUS of case 24 to retract.

†13 0-6 7=6 3+13 0=48 4%

28 0-25 0=3 0+5 0=10 7%

41 0-31 7=9 3 13 0-6 7=6 3+9 3=67 7

surface of the uterus of monkey 21. The fetus, membranes and placenta have been removed. The two lips of the cervix are apparent as ridges crossing the uterus at its extreme lower extremity and about 2 centimeters above this, respectively. The thickened "ring" above these ridges is the physiological retraction ring. The lower edge of the anterior placenta is seen to extend precisely to this ring, which marks the junction of lower and upper uterine segments. The posterior placenta was seen to have been placed somewhat laterally, but its lowermost extremity likewise reached just to this ring. In this specimen the maximum retraction of the isthmus posteriorly is readily evident.

In the consideration of results, the exact proportions of the term uterus prior to the onset of labor have not been estimated. The 3 animals which were sacrificed prior to

labor were of smaller stature than the others of this series. In addition, the fetal proportions indicated that the animals were in late pregnancy, but not yet at term. The early first stage measurements are therefore taken as being representative of maximum term size of the uterus.

The results will be discussed under two general headings: (1) Changes in the uterus during labor, and (2) incidental pertinent observations. For the most part the results require but little discussion since the illustrations and tables are self-explanatory.

Changes in the uterus during labor. Stage I. During the first stage of labor there is only slight shortening in the total internal sagittal circumference of the uterus. The dimensions of the cervix and the position of the cervical lips with respect to the true conjugate are similarly not altered significantly—this despite

TABLE VII—THE PER CENT OF THE TOTAL INTERNAL LONGITUDINAL CIRCUMFERENCE CONTRIBUTED BY THE CERVIX, ISTHMIC SEGMENT, AND CORPUS AT THE DIFFERENT STAGES

Stage	Isthmus cm including internal lips A	Total external lips cm B	Total internal lips cm C	Circumference E.O. to E.O. without internal lips cm D	Circumference OIO to OIO including internal lips E	Circumference OIO to OIO without lips (E-C) F	Isthmus without internal lips		Corpus		Cervix	
							cm (A-C) G	%	cm (F-G) H	%	cm	%
Before labor (term?)	10 7	3 6	2 2	36 4	35 0	32 8	8 5	23 5	24 3	67 1	3 6	9 9
I	13 0	4 1	0	43 3	41 0	39 0	11 0	25 5	28 0	65 0	4 1	9 5
II A	6	4 8	1 3	34 9	31 ~	30 4	5 4	15 4	25 0	71 6	4 8	13 7
II B	5 2	4 1	1 1	30 1	7 4	6 3	4 1	13 2	22 2	73 7	4 1	13 2
II C	5 6	4 4	1 2	6 1	22 5	1	4 4	16 9	16 8	64 3	4 4	16 9
III	?	4 1	2 9	18 5	17 3	14 4					4 1	21 6

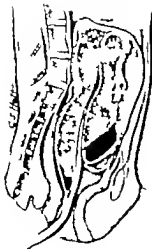


Fig. 2



Fig. 3

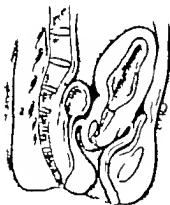


Fig. 4

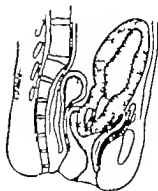


Fig. 5

chosen the lower border of the placenta as being at the approximate lower level of the corpus uteri. In addition to this in many of the specimens the uterine wall thickens abruptly from below upward at a level coinciding with the lower border of the placenta. This finding adds credence to the arbitrary division indicated above. The authors realize fully that this is by no means a precise indication of the upper boundary of the isthmus. Because of the constancy of the findings however it appears that this is a satisfactory means of indicating the activity of this portion of the uterus in contradistinction to the ac-

tivity of the corporeal segment and cervix. In full cognizance then of the possible fallibility of the indicated upper extent of the isthmus uteri we shall refer to the *isthmus segment* of the uterus as being that portion which lies between the internal lips of the cervix below and (1) the lower border of the placenta or (2) the region of a physiological retraction ring above. By these means of division of the uterus one may follow in successive specimens the activity of the *corporeal segment*, the *isthmus segment* and the *cervix*.

This means of differentiation is well shown in Figure 3 which represents the internal

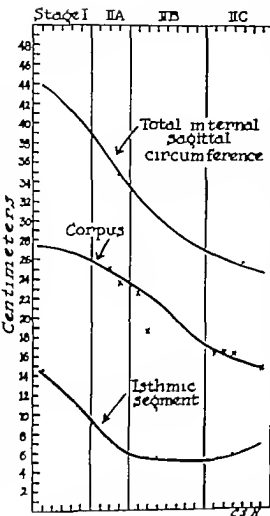


Fig. Graph showing the relative rate and extent of shortening of the total internal circumference of the uterus, of the corpus, and of the isthmus segment, during the first and second stages of labor.

the fact that dilatation is occurring.

the calculations in the tables, the 100 per cent measurement of the first stage is taken as an average of all first stage animals, whereas individual animals during the first stage showed progressive, significant isthmus shortening with no significant change in the corpus.

Stage II A During the early part of the second stage isthmus retraction progresses, and at this time becomes maximal. Progressive shortening of the corpus is now evident. There is no appreciable change in the length of the cervix during this period. The change in the level of the cervical lips with respect to the true conjugate however is marked. It is seen that during this substage the anterior lip of the cervix rises above the level of the symphysis. The posterior lip also rises significantly but not as extensively as the anterior.

Stage II B Obviously just prior to the birth of a part much descent of the fetus has occurred and this is reflected by an acceleration in the rate of corporeal retraction. Maximal shortening of the isthmus segment has already been attained and is sustained throughout this substage. The length of the cervix itself has undergone little change but the position of the lips with respect to the true conjugate shows further alteration. Anteriorly the external lip remains at a high level above the symphysis, and posteriorly the lip has reached the level of the sacral promontory.

Stage II C Examination of the specimens in this substage shows that after a part is born the uterus contains but little of the fetus, most being found in the vagina and that after half of the body of the fetus is born the uterus contains only placenta and amniotic fluid. Hence, much shortening of the entire longitudinal circumference should and does occur. It is of interest that throughout the

...the only evidence of longi...

rior lip averaging almost 2 centimeters above the symphysis, the posterior being located at about the level of the sacral promontory. The extent to which the cervical lips rise in the monkey is greater than that revealed by the frozen sections in the human being and also greater than that seen in the experience of obstetricians. Since the upward excursion of the cervical lips is limited by the fascial supports of the cervix (which include the pubo-cervical fascia and the transverse cervical and sacrouterine ligaments), it is apparent that in the monkey these supports are more flexible than in the human being. Caldwell and Stillman of the Sloane Hospital for Women have made preliminary studies which clarify this subject in the parturient woman. Metal clips have been placed upon the cervix and x-ray pictures made during the various stages of labor. Their studies indicate that the cervical lips pull up considerably higher than is generally believed, but not as high as in the monkey.

Stage III During the third stage there is continued shortening of the corporeal and isthmic segments. Cervical length, again, is not significantly altered. The almost instant return of the uterus to its general contour prior to the beginning of pregnancy is well illustrated by specimen No. 10, sacrificed one hour postpartum.

It has doubtless been observed that in this discussion of uterine changes during labor no mention has been made of the "thinning" which is believed to occur normally in the lower pole of the uterus. Our findings show that *longitudinal* thinning or actual stretching, does not occur normally in the isthmic segment in the monkey, with the single exception of the late second stage when the lower pole of the uterus relaxes to receive the placenta. All the evidence indicates that the region of the isthmus is not only the first portion of the uterus to undergo shortening in labor, but that, in addition, this shortening is progressive, and sustained until the late second stage. At cesarean section in the human being the illusion of thinning may possibly be produced by the contrast of the more marked and evident corporeal retraction, to the lesser but maximal retraction of the isth-

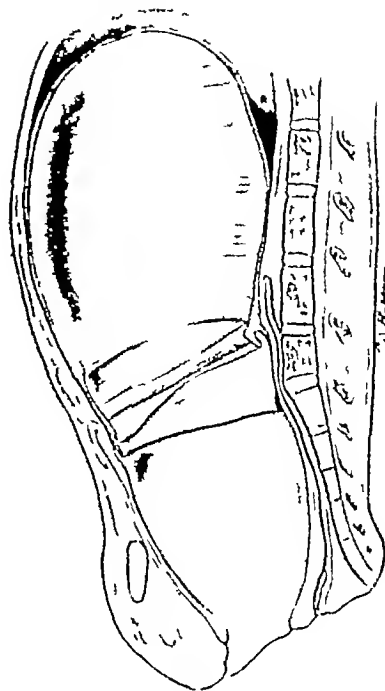


Fig 13

mus. Anesthesia may also be a factor. Actual longitudinal thinning of the isthmus may occur under certain circumstances in the human uterus, but we find no evidence of this in the monkey, nor have we found definite evidence of it in the human frozen sections in the absence of disproportion. In the instance of neglected disproportion the cervix is held fast by the taut cervical supports. Contractions of the powerful corpus uteri of necessity lead to longitudinal stretching with injury and ultimate rupture of the weaker lower pole of the uterus. The rupture of old cesarean section scars, often cited as evidence of isthmic thinning, occurs perhaps as frequently prior to, as during, labor. It is doubtless due to mecytasis or lengthening of the *circular* muscle, which occurs as the isthmus adapts itself to its contents during the second half of pregnancy, or as it enlarges laterally during early labor to allow the passage of the fetus.

Incidental observations The examination of the specimens brings to light many factors incidental to labor which heretofore have not been fully appreciated. Among these are

Uterine retraction of the corporeal musculature As may be observed in the illustrations retraction is quite even throughout the corpus in the first and third stages, and fairly so in the early second stage. In the late second stage however retraction is grossly unequal in the various parts of this structure. Certain of the human frozen sections, notably many of those of Canton and Gonzalez, show similar inequality of corporeal thickness at this time.

Excursion with ultimate complete obliteration of the vaginal vaults As the cervical lips rise in the pelvis, so must the vaginal fornices rise. This accordion-like action of the vagina is perhaps not fully appreciated. Its tremendous distensibility is well illustrated in Figures 9 and 9a.

Evidence of beginning separation of the placenta before completion of the second stage If a monkey is unrestrained in the third stage of labor she will pull upon the umbilical cord immediately after the birth of the fetus, to remove the placenta. If it does not come away after the first pull, it generally does so after a few minutes. This indicates that in the monkey the placenta is almost completely separated at the end of the second stage of labor. This is verified by our sections. Early separation of the placenta has often been postulated in the human being but there is no definite evidence either supporting or refuting it. In favor of such a postulation is the recent confirmation by Steer and Sullivan in a large series of cases that the placenta may be delivered almost invariably within 2 to 3 minutes after the baby if a Credé maneuver is performed at the moment when the uterus first adapts itself to its suddenly diminished contents. This observation has been made by numerous other workers since its original presentation by Chantreuil in 1870, following the suggestion of Credé.

SUMMARY AND CONCLUSIONS

1. The present understanding of the anatomy of the nonpregnant and early-pregnant uterus has been outlined. The necessity of considering the isthmus uteri as an important and distinct part of the uterus has been emphasized. The terminology used and is based on anatomical principles and

on comparative anatomical and physiological observations.

2. Frozen sagittal sections of 30 *Macaca rhesus* monkeys at consecutive chronological phases of late pregnancy labor and the puerperium have been made. Reproductions of 10 of these and of 1 of 3 nonpregnant animals are here presented. The entire series has been thoroughly studied with the view to determining the precise changes which occur in the laboring primate uterus. The conclusions recorded are based upon the analysis of the entire series of animals. All of the available human frozen sections have been similarly analyzed. The latter are not presented at this time. Although the human specimens were not satisfactory for the observation of many of the details, one receives the definite impression that the findings in the monkey are for the most part characteristic of those occurring in the human being with only a few minor quantitative differences. Our observations concerning the changes in the human uterus are generally in agreement with the models prepared by Dickinson and Belskie which are based upon a similar analysis of the human frozen sections.

3. In the first stage of labor retraction is limited chiefly to the isthmus uteri in the monkey. The intrinsic dimensions of the cervix do not alter appreciably despite the facts that dilatation occurs and that the lips rise to a slightly higher level in the pelvis. The total internal circumference of the uterus and the internal circumference of the corpus show only a slight amount of reduction in the first stage.

4. In the second stage of labor in the monkey the cervix rather quickly retracts to or above the true conjugate. Obviously this elongates the vaginal portion of the birth canal. On the basis of the total internal circumference retraction in the corpus and isthmus is at a proportionally similar rate during the early portion of the second stage. Maximal isthmic shortening occurs early however and is sustained until this segment relaxes to receive the placenta. The corpus, on the contrary

to manifest progressive shortening as the fetus which becomes especially large as a part is born

5 The cervical lips ascend to a higher level in the monkey than in the human being

6 The question of "thinning out of the lower uterine segment" is discussed briefly. Longitudinal lengthening of the isthmic segment does not occur in the monkey, and human frozen sagittal sections do not support its occurrence in this species in the absence of disproportion. The isthmic segment does seem relatively thin in contrast to the corpus which lies above. The latter is more bulky to begin with, and it is possible that this may lead to the clinical impression of a "thinned out lower uterine segment," whereas, in reality, the isthmus is undergoing perceptible longitudinal shortening. Our material allows no conclusions concerning the activity of the circular muscle of the isthmus during labor. Obviously, however, definite circular lengthening of the lower pole of the uterus must occur in order that the fetus be allowed to pass. Circular lengthening, then, may account for thinning in the lower portion of the isthmic segment. However, this does not explain thinning as it is commonly thought to occur throughout this segment.

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RECURRENT FRACTURE

WILLIAM A. EVANS, J. M.D. Detroit, Michigan

IT is commonly believed that when a fracture heals without deformity the bone structure at the fracture site is as firm if not more so than before. This certainly seems to be true in most instances. Fractures which recur at the site of a fracture deformity or of an old pathological process where there is structural weakness are easily understood and do not call for comment. Such recurrent fractures were apparently frequent in the time before Roentgen and Lister when wound infection and the inaccurate reduction of fracture deformities were more common. There is, however, a group of cases deserving consideration in which the cause of refracture is not as apparent.

Small groups of these cases have received comment in the European literature. Troell, in 1917 reported 4 cases and mentioned a few others. He pointed out that the new fracture is never an anatomical copy of the old one even when the latter is not completely healed. Disease atrophy and foreign bodies at the fracture site were thought to predispose to refracture. His cases included (1) a 50 year old man with a fracture of the humeral shaft showing complete healing after operative reduction and then refracture 5 months later (2) fractures of the mid radius and ulna in a 12 year old patient reduced by open operation and ivory implants, and a refracture 7 months later (3) 2 fractures of the femoral neck occurring 6 years apart in a 65 year old male and (4) 3 fractures of the tibia the third one occurring 13 years after the other two in a 31 year old male.

Peritz, in 1927 reported 6 cases in children between 9 and 16 years of age of whom were siblings. The children were otherwise healthy and there had been no other fractures. The interval between the fractures was from 3 weeks to 33½ months. As a possible explanation she gave deficient callus production at the first fracture site due to the very limited injury to the periosteum. Two of the fractures were subperiosteal in type and there was formation of calcium-poor zones, such as are seen in hunger osteopathy and the so called "chronic" fracture. Other factors considered were late results of starvation during the war and an avitaminous of the winter months,

inasmuch as the cases appeared at that season of the year. It was further noted that all fractures had occurred in the mid-diaphysis and it was believed that an injury to the nutrient artery and the resultant changes in the bone might be a basis for refracture.

Struss and Mandel, in 1932 reported 7 patients with fractures recurring after intervals of 4, 7, 3, 16, 38, 32 and 36 weeks. The patients were between 6 and 27 years of age—3—14, 17 and 6 years of age—had fractures in the forearm, 3 in the lower leg, and 1 in the thigh. Although the fractures recurred at the exact sites of the old fractures, they pointed out the slightly different character and configuration of the fracture lines. They regarded refractures of this type as very rare and considered malnutrition as a factor in their causation.

Slavero, in 1939, has reported 16 cases of refracture but most of these occurred in cases in which there was much deformity at the first fracture site or in which the first fracture had been complicated by infection. In 6 instances, however the basis for refracture was not so readily apparent. These patients were 13, 12, 11, 16, 13, and 33 years of age and the fractures had recurred after intervals of 8, 11, 6, 5, 21 and 22 sets, respectively.

The x ray was used very sparingly and, in some of the cases, it would appear that the healing of the fracture had not been complete. The author gives the general causes of defective healing which are well known but has regarded fractures of the forearm in children as a special instance. Here the fractures may be subperiosteal with insufficient injury to the periosteum to cause callus formation or there may be injury to nerve or nutrient artery as possible basis for the refracture.

MATERIAL

In a study of refracture, one may first consider a group of cases in which there is some demonstrable and reasonable basis for the second fracture. We have encountered instances of generalized and local pathological conditions of bone which predisposed to refracture and one instance in which a fracture had recurred many years after the implantation of a foreign body in the successful repair of the first fracture.

Multiple fractures are a well recognized feature of osteogenesis imperfecta, but perhaps less well recognized is the tendency for the fractures to recur at the same site in different bones. This is well illustrated in Case 1 in which there were multiple fractures of both femora and of the right tibia, the recurrent fractures appearing at, or near, the old fracture sites. This is in part due to the deformity with which healing occurred, resulting in a structural weakness which predisposed to a refracture at that point. In other instances, however, it would appear that the healing of the fracture had occurred with the formation of particularly fragile bone in that area and this seems to be borne out by the character of the recurrent fracture line.

Recurrent fractures in an area of pathological bone structure and at the site of a foreign body are readily understood and are well illustrated by Cases 2 and 3. Nevertheless, it is of interest to observe that although the healing of the first fracture in Case 2 was apparently quite normal, in reality an osteitis fibrosa had developed and was not discovered until the time of the second fracture. In Case 3 there was without doubt a fragility of the bone structure about the bone screw implants, but this was not evident from an examination of bone structure by x-ray either at the new fracture site or of the intact bone about the proximal screw. Not only had there been no absorption of bone about the screws, but the bone was unusually dense.

The largest group of cases in this series is made up of those having recurrent fractures of the bones of the forearm. Others have commented on the peculiar liability of fractures involving the shafts of the radius and ulna in children to recur, and this is borne out by the fact that we have encountered 8 such cases although this is not one of the most common sites of fracture either in children or adults. The most common fracture in children is at the lower end of the radial diaphysis, 1 to 2 centimeters proximal to the distal epiphyseal line. No instances of a refracture in this area were encountered, and it may be inferred that here healing takes place with the formation of a bone structure more solid than before. This idea receives some support from Cases 16 and 17, in which a Colles' type of fracture was followed after a short interval, in 1 instance only 3 months, by a second injury with fracture in the forearm. Although the type of injury seemed to be due to the same mechanical forces, the second fracture did not occur at the old fracture site which would have been the case if that were a *locus minoris resistentiae*, but rather in the shaft

some distance proximal to the old fracture site.

The 8 cases with recurrent fractures in the mid-portion of the shafts of the radius and ulna give evidence that in children, at least, healing of fractures in this area may fail to restore the bone to its original strength. The altered character of the bone structure after healing is shown by the peculiar configuration of the second fracture lines which was observed in all instances and suggests an abnormal fragility of the bone. These second fracture lines resemble the fracture lines seen in osteogenesis imperfecta, as well as the fracture lines observed in rickets and the "insufficiency fracture" described by Hansson and others.

One reason that has been suggested for the increased fragility in these cases is an involvement of the nutrient foramen and a consequent impairment of the blood supply to the bone. This is conceivable in Cases 4, 6, 10, and 11, but would not apply to Cases 5, 7, 8, and 9, in which the fractures have occurred at some distance from the positions usually given for the nutrient foramen. Nevertheless, it is possible that in the shaft where the cortex and medulla are sharply differentiated, the blood vessels or nerves may be more seriously injured than in the cancellous portions without actual involvement of the foramen.

Other possibilities for the fragility of the bone are the complications present during healing in some of the cases: a pressure ulcer in the skin of Case 4, a respiratory infection and incomplete immobilization of the arm in Case 7, chickenpox in Case 9, and soft tissue atrophy in Case 10.

A further possibility is a constitutional peculiarity of these children. Many of them tended to be undernourished, and the extremities were strikingly thin and wiry. Six of the 8 were definitely below the average weight for their age and height and were described as "poor eaters" and "delicate," as compared with their brothers and sisters. A mild form of osteogenesis imperfecta is suggested by the thin bluish sclerae and the hyperflexibility of the ligaments which many showed.

In the treatment of fractures of the forearm in children, where the shafts of the radius and ulna are involved, it seems advisable to recommend that these children, and those responsible for their care, guard against the possibility of further injury even after recovery seems complete. The liability to refracture might also be lessened if the food intake could be increased and the nutritional state improved.

Comparable in many respects to the 8 cases of refracture in the radius and ulna are the 2 cases (12 and 13) of refracture in the clavicle. The

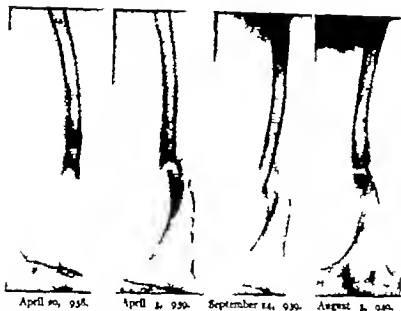


Fig. Case. Severe osteogenesis imperfecta with numerous fractures of the bones of both legs. Fractures occurred in the left femur in April, 1934, April, 1935, April, 1935 and August, 1940. All of these fractures took place at the same site in the femoral shaft after osseous union had occurred.

shafts were involved where the cortex and medulla are sharply differentiated and near the nutrient foramen. Both children suffered upper respiratory infections during the period of healing and the character of the second fracture lines indicated an abnormal fragility of the bone. Some features of osteogenesis imperfecta were observed in Case 2 and this patient was below the average weight for his height and age.

Two cases remain which present certain new features and raise new questions. Case 14 is not strictly pertinent to this study for although the 2 fracture sites in the tibia appear identical, the growth of the bone during the interval of 6 years has displaced the old fracture site some distance distal to the new fracture site. Thus we are not faced with a true exception to the observation that refractures occur in the compact structure of the shaft rather than in the spongy areas at the ends of the long bones. Case 5 concerns a very obese boy of 18 who sustained 3 fractures in the same area of the fifth metatarsal bone with intervals of 5½ months and 4½ months between them. The fractures were each

preceded by a definite acute trauma producing severe pain and each injury was sustained in a slightly different way under different circumstances. March fractures usually involve the second metatarsal bone although Koch has described one in the fifth metatarsal in a deformed foot. Furthermore Watson Jones states that metatarsal fractures due to muscle strain may recur. Although the obesity in this instance may have been productive of muscle and bone strain, an invidious history of progressive pain without acute injury which is characteristic of march foot is quite unlike the history in this case. The rather short interval between the fractures suggests that healing may not have been complete at the time of the refracture. This is contradicted, however, by the facts that the patient made a complete clinical recovery after each fracture using his foot in a normal manner again without pain and that the new fracture lines were of slightly different configuration than the old ones.

FURTHER FACTS ON RECURRENT FRACTURES

Upon the observation of a recurrent fracture, the question arises as to whether the healing of the first was complete. In some of the cases the x-ray studies indicated complete healing and in all cases there was clinical evidence of healing

A study of the chart in a monograph of the Society for Research in Child Development (16) giving the growth in length of the tibial shaft during childhood indicates an average growth of 3 centimeters in the interval between the fractures. Assuming a growth of 3 centimeters at each year would bring the new fracture well proximal to the old fracture site. Inasmuch as the child in Case 14 was very close to the average weight and height and the growth of the tibia almost equal at each end, the assumption seems valid.



Fig. 2. Case 1. Similar changes are seen in the right thigh where fractures of the femur are known to have occurred in June 1937, April 1938, August, 1938, and (?) September 1939.

as indicated by normal use of the part without pain. The interval between the fractures, although in some instances barely over 3 months, exceeded the period generally considered necessary for healing in uncomplicated cases. However, the available clinical evidence of complete healing of human fractures is admittedly not entirely adequate and for further information one must turn to animal experimentation. Lindsay and Howes, in 1931, reported studies on the breaking strength of healing fractures in the fibulas of rats. They quote Leriche to the effect that the healing rate in bone was the same for all animals that he studied so that their results may have an applicability to man. They found the breaking point of the rat fibula to be at a strain of from 285 to 580 grams. During healing, strength first appeared at the fracture site on the sixth day and there was a rise in strength to an average resistance of 341 grams at 21 days. This was followed by a slight fall to 277 grams on the thirty-third day and a subsequent rise to 465 grams at 45 days. At this time the bone at the fracture site was as firm as elsewhere and there was no predilection for the fracture to occur at the old fracture site. The first peak of healing strength coincided with the maximum extent and density of the callus and the subsequent fall was correlated with the absorption of the callus surrounding the bone and in the medullary canal. Further observations (6-9) with the rats on various diets showed most consistently that changes in the quantity of food consumed and the rats

weight exert a strong influence on both the healing and the normal breaking strength of the fibulae. The greatest loss of strength was noted on a high carbohydrate diet with lesser changes on a high fat low calcium diet. Maximum healing strength was obtained in about 45 days on all diets.



Fig. 3. Case 1. The right femur with recurrent fractures of the femur on November 9, 1938, September 14, 1939, and December 18, 1939.



December 7, 1931. March 13, 1932. July 9, 1932.

Fig. 4. Case 2. T recurrent fractures in the shaft of the right tibia in French-Canadian boy who sustained the original fracture on November 5, 1931, at the age of 3 years and 7 months. The original films are not available but the report indicates an abnormality in the bone structure at the fracture site at that time. The healing was apparently satisfactory although cystic formation was discovered at the time of the second fracture on December 7, 1932. A third fracture occurred on July 9, 1932, and this was followed by surgical exploration with diagnosis of osteitis fibrosa cystica on the material removed for pathological study.

Haebler and Reles, in 1936 made studies on the tension and bending strength of excised canine long bones. No relation could be established between the flexibility to bending or tension and the age, weight, length, or in the calcium or water content of the bone. This is admittedly in contrast to man in whom the fragility of bones in the aged and the flexibility of the bones in the child are well recognized. Marked differences were found in different bones of the same animal. In studies on healing fractures they found that the extent and density of the callus as demonstrated by x ray may be misleading in estimating the strength at the fracture site and there was no close correlation between the calcium content of the dried material at the fracture site and the firmness of healing. Water content seemed to be of considerable importance. They believed the best evidence of healing to be painlessness under strain.

The effect of the diet and vitamin intake on the healing of fractures has been subject to much



August 23, 1934. September 3, 1934. August 1, 1935.

Fig. 5. Case 3. Recurrent fracture of the femoral shaft in an 8 year old boy 5 years after the original fracture which was treated by open operation and the implantation of two bone screws.

study. A review of this material was published in a monograph by Hertz, in 1936. Recurrent fractures during attacks of scurvy were reported in sailors by Richard Walter in 1740, Mead in 1763, Marriquet in 1783, Bell in 1788, Callison in 1793, Hammick in 1830, Budd in 1840, and Moore in 1859. Israel and Fraenkel studied this phenomenon experimentally and found that scurvy may soften a callus already formed and facilitate refracture. Their findings were supported by the experiments of Schlowzew and contradicted by those of Roegholt. Hertz made experiments on scorbutic guinea pigs and could not substantiate the conclusions of Israel and Fraenkel. Thirteen animals with fractures of the fibula were placed on a scorbutic diet after 35 days, and they died in from 54 to 7 days. All of the fractures were found well healed. Hunger osteopathy and the occurrence of a chronic fracture as the result of mechanical strain are offered as an explanation for the observations in scorbutic sailors and in the animals studied by Israel and Fraenkel. Delayed healing of fractures in subjects deficient in vitamins A, B, and D has been reported. In the cases of recurrent fracture which we have studied there was no evidence of vitamin deficiency either in the history of food intake or in the appearance of the bone structure. However an impressive number of the patients were underweight and had poor appetite so that possibility of some food deficiency and dietary osteopathy must be considered.

A number of papers have appeared, chiefly in the foreign literature on the occurrence of in-

sidious or chronic fracture. The best examples are the march foot and the fissure fracture of the tibia which are prone to occur in young military recruits subjected to unaccustomed strain. Cases have been described and discussed by Koch, Olsson, Reischauer, Hansson, Pfahler, and others. It is generally agreed that there is no acute trauma, but that under the influence of prolonged strain a periosteal proliferation occurs followed by the appearance of a fissure in the cortex. The symptoms are insidious in onset and progressive in character. The first x-ray studies may be negative as the callus does not become demonstrable for 8 weeks or more (Koch). Fractures of this type also are seen in undernourished individuals as a manifestation of a hunger osteopathy or rickets. Although the fracture lines bear a certain resemblance to the refractures seen in this study, an identity cannot be established, for in all of our cases the refracture was accompanied by a very definite history of acute trauma, and there was no deformity or habit of behavior productive of a chronic strain. Furthermore, the old fractures were symptomless at the time of the refracture.

CONCLUSIONS

1. Fractures are prone to recur when a general or local disease of the bone is present, when healing has occurred with deformity, and at the site of a foreign body. The basis for such fractures is readily understandable.

2. A fracture may also recur at an old fracture site after healing has apparently been complete and in the absence of a significant deformity or recognizable complicating pathological process.

3. The character of the new fracture indicates an abnormal fragility of bone at old fracture site.

4. Recurrent fractures of this type are most often seen in the shafts of the radius and ulna of children. Such children are apt to have poor appetites and to be of less than average weight with thin extremities. The flexible ligaments and blue sclerae which many of them show suggest a constitutional background in common with osteogenesis imperfecta.

5. It seems desirable for children who have had fractures of the shafts of the radius and ulna to take particular care against a second injury even after the healing of the first injury appears complete and to increase their food intake for the improvement of their nutritional state.

CASE REPORTS

CASE 1. M. S., C. H. D. 3140. A white female of English nationality born on March 15, 1932, was first seen at the



Fig. 6. Case 4. Recurrent fractures of the left radius and ulna in a 9 year old boy after interval of 1 year and 1 month. First view shows appearance of healing at fracture sites 6 weeks after the first injury. Healing was complicated by a pressure sore but recovery was eventually complete. Second view showing new fractures of different character at the old fracture sites.

Children's Hospital in April, 1938, having recently sustained a spontaneous fracture of the left femur. The dates of previous and subsequent fractures are as follows: the left femur in April, 1933, April, 1938, April, 1939, and August, 1940, the right femur in June, 1937, April, 1938, August, 1938 and (?) September, 1939, the right tibia in November, 1938, September, 1939, and December, 1939.

On May 28, 1938, the neck was explored surgically and a parathyroid gland somewhat larger than usual, encountered at the right lower pole of the thyroid gland, was removed. Microscopic study of the specimen revealed nothing remarkable and the operation had no demonstrable effect on the patient's course. Theelin was given for a period without effect. An x-ray study of the spine in September, 1939 showed a low mineral content of the bone structure and the vertebral bodies had a marked bi-concave configuration as the result of expansion of the intervertebral discs. Multiple fractures of the ribs were also noted. The fractures of the left femur are illustrated in Figure 1 and show the tendency to recurrence in the areas of abnormal bone structure at the old fracture sites. The condition has been regarded as an osteogenesis imperfecta and except for the deformities incident to that, the physical examinations have not been remarkable.

CASE 2. R. P., C. H. 92720. This boy, born of French Canadian parentage on April 25, 1930, was first seen at the Children's Hospital in 1932 for bronchoscopic removal of a peanut. He was next seen on December 7, 1938, giving a history of falling while chasing another boy and injuring his right leg. It was later learned that a fracture had



Fig. 7. Case 5. Recurrent fractures of the right radius and ulna in a 7-year-old boy after an interval of 5 months. The first two views show the first fractures with the appearance of satisfactory healing after 4 months. The second fractures are at the old fracture sites but are of different character.

occurred in the right tibia 5 years previously followed by satisfactory healing. X-ray studies here in 1938 (Fig. 4) showed an oblique fracture through an area of cystic disease in the middle third of the tibial shaft. There was no deformity as a result of the fracture and cast as pulled for 7 weeks. Healing occurred and the normal use of the part as regulated although the area of pathologic bone structure persisted.

On July 6, 1939, he fell again, sustaining another fracture in the right tibia with fracture lines similar but not identical to those observed previously. Healing was again occurring but it was decided to curette the cystic area and fill the cavity with bone chips. This was carried out on October 4, 1939, and pathological study of the material removed showed the characteristic appearance of osteitis fibrosa cystica. Satisfactory healing occurred with an uneventful recovery and subsequent roentgen-ray studies on October 31, 1939, December 26, 1939, March 2, 1940, and May 4, 1940, and November 2, 1940, revealed increasing solidity of the bone structure with new areas of cyst formation.

CASE 3. J. S. C. H. 746 This patient, of French-Syrian parentage, born on July 6, 1935, was struck by truck which passed over his left leg on August 7, 1934. A comminuted fracture of the lower tibia was recognized and treated accordingly. On August 26, 1934, deformity of the left thigh was noted and long oblique fracture of the femoral shaft was discovered (Fig. 5). The fragments were

overriding about 3.5 centimeters, and there was callus at the fracture site, giving an appearance compatible with the date of the first injury. Because of the deformity an open reduction was performed with removal of the callus, resection of the sclerotic ends of the fragments, traction, and correction of the overriding. With the fragments in close end-to-end approximation two bone screws were inserted. A plaster cast was applied for 8 weeks, at the end of which there was good union, as reported.

There was no disability or complaint until August 20, 1939, when he jumped about 1 foot from the roof of a garage and experienced pain and swelling in the left leg. X-ray studies showed that there had been complete break at the old fracture site in the femur. With no demonstrable osseous change about the bone screws. However, a new fracture had occurred involving the site of the more distal screw. With somewhat different configuration and character of the fracture line. After unsuccessful attempts at manipulation, an operation was performed on August 26, 1939, and the lower screw which lay between the fragments, was removed. The upper screw was firmly in place and could not be moved. Tantalum Purkin bands were applied with the fragments in close end-to-end approximation. Healing occurred rather slowly and on April 2, 1940, he was allowed up on crutches with a cast brace. On October 6, 1940, the brace was removed and there was no pain or disability in walking except for a very slight limp.

At an interview on November 2, 1940, the patient was observed to be as active, well nourished, and well developed boy weighing 33.5 kilograms for height of 57 cent.

The X-ray report from another hospital dated November 21, 1939, describes an oblique fracture of the middle third of the right tibia. No mention made of any cystic formation.

meters. There had been no other fractures than those here described, and in a family of 5 other siblings only one fracture had occurred and that was sustained in an auto accident. The diet had been adequate and well balanced. The sclerae appeared bluish but there was no deafness or abnormal flexibility of the ligaments.

CASE 4 S A, C H C 2530 This Armenian boy, born on March 2, 1931, fell while climbing the back of a chair and injured his right arm in April, 1937. The x-ray studies revealed greenstick fractures of the midradius and ulna. Following manipulation and immobilization satisfactory healing occurred without deformity or disability.

On July 22, 1939, in a fight over a toy wagon, he was attacked by another boy and the two fell to the ground on his outstretched left arm. X-ray studies made in Providence, Rhode Island, showed fractures of the middle thirds of the left radius and ulna with lateral and anterior angulation at the fracture sites. The deformities were reduced, and a fixation dressing was applied. On August 7 a large pressure sore was discovered and a new dressing was applied. On his return to Detroit, x-ray studies were made at the Children's Hospital on September 5, 1939 (Fig. 6), and the fracture sites are well shown with bony union occurring in a satisfactory manner. The child recovered the use of his arm completely.

Enlarged tonsils were removed on April 22, 1940, and at that time the physical examination was otherwise negative.

In August, 1940, while boxing he was tripped by his opponent and fell backward on his extended left wrist. X-ray studies on August 12, 1940 (Fig. 6), showed new fractures in the middle thirds of the left radius and ulna. It was evident that complete healing had occurred at the old fracture sites and the new fractures, although occurring in the same area, had a slightly different configuration of the fracture lines. Following manipulation, healing again took place.

The boy appeared quite thin and very active, weighing about 24 kilograms with a height of 131 centimeters. This is a constitutional type shown by his parents and a sister. He was described as a "poor eater" but with no peculiarities of taste and with a good vitamin intake. No fractures other than those described have been sustained by him or his family. The sclerae were rather thin but not definitely blue. There was no deafness. The ligaments about the joints were quite flexible but not abnormally so.

CASE 5 W S, C H 118080 A male child, born January 15, 1933, of German extraction, was first seen at the Children's Hospital in November, 1936, when a tonsillectomy was performed for large tonsils. The physical examination was otherwise negative. On November 26, 1939, he was pushed from a porch by his brother and sustained fractures of the right radius and ulna (Fig. 7). The deformity was reduced by manipulation, and immobilization in plaster was carried out for 10 weeks. Frequent x-ray examinations revealed satisfactory progress in healing, and on March 26, 1940, healing was thought to be complete. The clinical findings confirmed this, and the boy made free use of his arm without complaint.

On April 28, 1940, 5 months after the previous injury and 2½ months after free use of the arm was allowed, he sustained a new injury to the right forearm in a fall while jumping during a game. The x-ray examinations revealed new fractures of the radius and ulna at the old fracture sites. There was, however, a slightly different configuration of the fracture lines. Immobilization in plaster for 7 weeks resulted in satisfactory healing at both fracture sites.

At an interview on October 16, 1940, the x-ray examination showed complete healing with minimal de-



February 23, 1940 March 11, 1940 June 27, 1940

Fig. 8 Case 6 Recurrent fractures of the right radius and ulna in a poorly nourished, 7 year old girl, after an interval of 4 months and 2 weeks. Healing of the first fractures seemed satisfactory clinically and by x-ray on March 11, 1940, 2½ weeks after the injury. The second fractures are distinctly different in character and delineation although occurring at the old fracture sites.

formity, and there was free use of the arm without discomfort. He appeared to be a rather thin and very active boy, weighing 27 kilograms with a height of 129 centimeters. He had suffered no fractures other than those described but gave evidence of many minor cuts and bruises. There was no deafness but the sclerae were slightly bluish and the ligaments were of somewhat more than average flexibility.

CASE 6 L D, C H 105617 A girl of Irish parentage, born on December 12, 1932, was first seen in the Out Patient Department in 1934, with eczema. She complained of a prolonged cold with cough in 1939 and much enlarged tonsils were found. The tuberculin skin test was negative.

On February 16, 1940, her right arm was pulled violently while playing with an older girl, and an x-ray examination 1 week later revealed transverse fractures of the middle thirds of the radius and ulna, the only deformity being a slight anterior angulation at the fracture sites. Immobilization in plaster was carried out for 6 weeks, and there was the usual progress in healing observed clinically and by x-ray. At the end of 6 weeks she was allowed free use of the arm and, although writing with the right hand, she continued to use the left for eating and striking other children.

The second injury occurred on June 27, 1940, in a fall from a bicycle, and new fractures of the right radius and ulna were observed at the old fracture sites with, however, a slightly different character and configuration of the fracture lines. Following manipulation the right extremity was placed in immobilization in plaster for 9 weeks and there was again satisfactory progress in healing of the bone at the fracture sites.

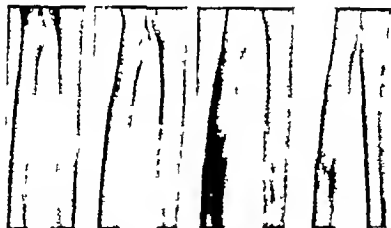


November 9, 1935. February 24, 1936. January 9, 1939.

Fig. 9. Case 7. Left forearm of male child, no sustained fractures of the radius and ulna on 4 occasions—November 9, 1935; December 29, 1935; January 9, 1939, and August 24, 1939. On the first occasion healing as

March 9, 1939. August 24, 1939. October 7, 1939.

complicated by an upper respiratory infection and incomplete immobilization. There is good functional recovery and no deformity following the second, third, and fourth injuries.

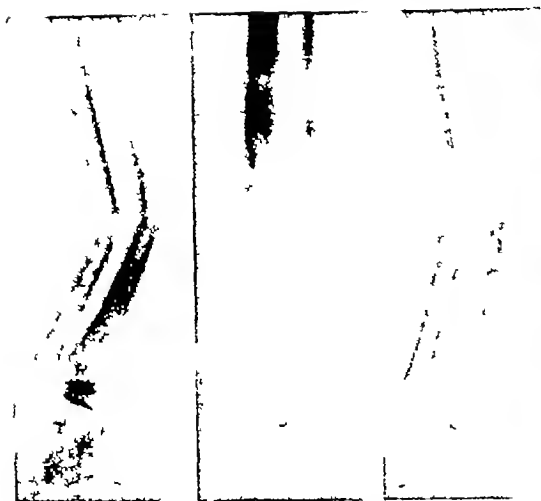


September 4, 1937. November 4, 1939. December 2, 1940. December 28, 1940.

Fig. 10. Case 8. Recurrent fracture of the left radius in poorly nourished 7-year old girl after an interval of 3 years and 3 months. At the first injury both the radius and ulna were involved and healing as observed to be complete 7 years later on November 4, 1939. The second fracture of the radius occurring at the injury of November 2, 1940, as inconspicuous in the study of December 2, 1940, but is confirmed by the appearance of callus on December 28, 1940.

The patient was interviewed on October 6, 1940. There is free use of the arm without deformity or disability and the X-ray examination revealed complete healing at the fracture sites. She is observed to be an unusually small

and thin, but very active girl, weighing 25 kilograms (55 lb.) height of 120 centimeters. This was constitutional trait shared by the mother and her other children. She had suffered no fractures other than those described and only



November 20, 1940 November 20, 1940 March 1, 1941

Fig 11 Case 9 Recurrent fractures of the right radius and ulna in a 7 year old girl after an interval of 3 months and 1 week. Healing of the first fracture was complicated by chicken pox but appeared complete with no deformity or disability. The second fractures, although at the old fracture sites, have a different course and character.

one other fracture in the family was recalled. She had been examined recently in the medical clinic, but no cause for her low weight was discovered. Her mother described her as a poor eater but there were no fancies or peculiarities of the diet. There was no deafness but the sclerae were thin and slightly bluish and there was more than usual flexibility at the joints.

CASE 7 M S, C H E 286 This boy, born of Irish parentage on December 14, 1933, was seen at another hospital on November 11, 1935, the day following a fall out of bed and an injury to his left arm. The x ray studies (Fig 9) disclosed fractures of the midradial and ulnar shafts. Further study after the application of a plaster dressing showed an excellent end to end approximation of the fragments and a good alignment except for slight posterior angulation at the radial fracture site. The records do not reveal the length of the period of immobilization, but there is a note that on December 7, 1935, the cast was cut and passive motion applied. Convalescence was prolonged and complicated by an upper respiratory tract infection without elevation of temperature and with a negative x-ray study of the chest on December 10, 1935, and he was not discharged from the hospital until December 22, 1935.

Six days later he fell while playing and again injured the left arm. X ray films showed new fracture lines at the old fracture sites and a rather marked degree of posterior angulation. Following manipulation and immobilization in an excellent position and alignment of the fragments was observed at the roentgen studies of December 29, 1935, January 25, 1936, and February 24, 1936.

Recovery was apparently complete and he had normal use of his arm until January 10, 1939, when he was pushed from a bed while playing with his sister and sustained a new injury to the left arm. Fractures were again seen in the radius and ulna at the old fracture sites. The disalignment was corrected and immobilization in plaster was maintained for 10 weeks. Good use of the arm was re-



June 27, 1940 August 22, 1940 February 9, 1941

Fig 12 Case 10 Recurrent fractures of the left radius and ulna in a 14 year old girl after an interval of 7 months and 2 weeks. Healing of the first fractures was complicated by considerable atrophy, but there was no other deformity and good function was obtained. The second fracture lines are of distinctly different character than the first, although occurring at the same sites.

gained and the clinical impression on April 18, 1939, was that the fracture was completely healed. On June 12, 1939, his foot became caught in a bicycle. Pain persisted and an x ray examination on June 15, 1939, revealed a greenstick fracture at the lower end of the tibia. Immobilization in plaster was carried out for 6 weeks and satisfactory healing occurred.

On August 24, 1939, he sustained a fourth injury to his left arm when pushed by some boys at play and for the fourth time a fracture was demonstrated in the midradius. The ulna appeared intact at this time. Satisfactory healing occurred with immobilization in plaster for 9 weeks.

At an interview on October 16, 1940, the boy was observed to be very active physically and mentally. He weighed 22.5 kilograms with a height of 117 centimeters and appeared well nourished. His mother had observed that in the past his wrists had appeared thin compared with those of his brothers and sisters and he had inclined to be "delicate" although he had recently become more robust. His diet seemed satisfactory and he had a good appetite, but he had small, poorly developed teeth. The sclerae appeared bluish and the ligaments were quite flexible at the joints but there was no deafness. He had sustained no fractures other than those described. One sister had suffered a fracture of the clavicle in an accident but no other fractures in the family were recalled.

CASE 8 R O'C C H C 4098 This girl, born of Irish parentage on October 24, 1930, was first seen at the Children's Hospital on June 14, 1937. She had large tonsils and an uneventful tonsillectomy was performed on July 18, 1937. On September 3, 1937, she fell about a foot while playing on a small tree stump, injuring the left arm and crying with pain for 2 hours. The x ray examination the



Fig. 3. Case. Recurrent fractures of the left radius and ulna occurring in 9 year old boy after an interval of 4 months and 2 weeks. The healing of the first fracture was complete by ray films February 4, 34 and by clinical examination, and free use of the part was regained. The different character of the new fracture lines at the old fracture sites as well shown.

next day showed transverse greenstick fractures in the middle thirds of the radial and ulnar shafts with slight palmar angulation at the fracture sites. After the manipulation plaster dressing was applied for 6 weeks. Satisfactory use of the part was obtained but for some time there was tenderness about the fracture sites and for a long time the part could ache during inclement weather. E on her recovery seemed complete. Her mother noted that she would tend to protect that arm. A second injury occurred on November 4, 1930, when she was struck in the posterior aspect of the lower part of the left upper arm. Swelling and ecchymosis appeared, and there was pain for a few days but the x-ray studies are negative and there was observed to be normal appearance of the bone structure at the old fracture sites, with no deformity. The arm was carried in sling for 3 weeks, and good recovery was obtained.

On November 22, 1930, she fell over 4 feet while playing on the edge of a sand pit, again injuring the left fore arm, and there was immediate severe pain causing her to cry for hours. The pain persisted and on December 3, 1930 she came to the clinic for x-ray studies. These showed a soft perosteal shadow about the middle third of the radial shaft at the old fracture site and a very slight disturbance in the bone structure such as not present at the examination of November 6, 1930. Re-examination on December 23, 1930, showed some resorption and increased density of the periosteal deposits and the irregularity of the bone structure as seen. Little more resorption so that there was no reasonable doubt that a second fracture of a very limited subperiosteal type had occurred at the old fracture site.

At the interview of December 28, 1930, there was no complaint of pain and she exhibited free use of the arm,

although her mother said that there was sometimes pain at night requiring hot water bottle. She had sustained no other fractures nor were there fractures in any of 6 siblings. Her appetite had been generally poor and she could knife for meat or vegetables. She was decidedly thinner and less robust than her healthy brothers and sisters. Her weight at this time was 36 kilograms for height of 35 centimeters. The ligaments about the joints showed more than the usual flexibility and the sclerae appeared thin with bluish cast. There was no deafness.

CASE 9. M. McK. A white girl born on March 25, 1911, and living in comfortable circumstances, tripped over her rubber while running on a playground at school and fell on her extended right arm on November 30, 1930. She was referred to us a few hours later as a private patient of Dr. Charles Kennedy and the x-ray examination disclosed greenstick fractures of the radius and ulna near the junction of their middle and distal thirds with sharp anterior and medial angulation at the fracture sites. Under ether anesthesia the normal alignment was restored, and plaster dressing as applied. Re-examination 14 days after the injury showed the fragments in close end to end approximation with an excellent alignment in both planes. The immobilization was maintained for 4 weeks and then as discontinued temporarily for early physiotherapeutic measures, extending over a period of 3 days, then the cast was discarded entirely. Convalescence was complicated at this point by an attack of chickenpox, but the normal use of the right arm was regained and there was no complaint or deformity of any kind.

On March 1, 1931, while roller skating she fell again on the right arm and sustained marked deformity as before. Refractures of the old fracture sites were demonstrated on the x-ray films but with slightly different character and configuration of the fracture lines. There was again marked angulation toward the radial and ulnar aspects.

At an interview on this date she was observed to be fairly well nourished blond girl of pleasing appearance and weighing 7 kilograms with height of 35 centimeters. The arms and legs were quite thin and there was more than the usual flexibility of the joints. Her mother described her as "poor eater" taking food very slowly and having no reason to eat. She liked variety of appetites, however and drank three glasses of milk daily. The sclerae were thin and there was no deafness. The patient had sustained no fractures other than those described and none had been experienced by her mother or 4 sisters. Her father has been involved in accidents with fractures of the nose and at the ankle.

CASE 10. E. W. This girl, private patient of Dr. Darrling of Pontiac, Michigan, was born on June 2, 1906. On June 7, 1930, while playing out of doors she jumped on a bench which tipped over and she was thrown to the ground on her outstretched left arm. Fractures of both bones of the forearm occurred, the ulnar fracture being quite oblique, with the end of the proximal fragment perforating the skin. X-ray studies (Fig. 1) on the same day showed the fractures with angulation anteriorly and toward the radial side particularly at the ulnar fracture site.

The deformity was reduced by manipulation and plaster dressing was applied and kept on for 6 weeks. The arm was markedly atrophied and remained thinner than the right one until the time of the second injury. There was no pain or other deformity, however, and the arm was used quite freely except for some slight limitation of pronation and supination. The puncture wound in the skin healed well and there were no signs of inflammation or infection.

She attended school during the autumn in good health and engaged in all of the usual activities. On February 9,

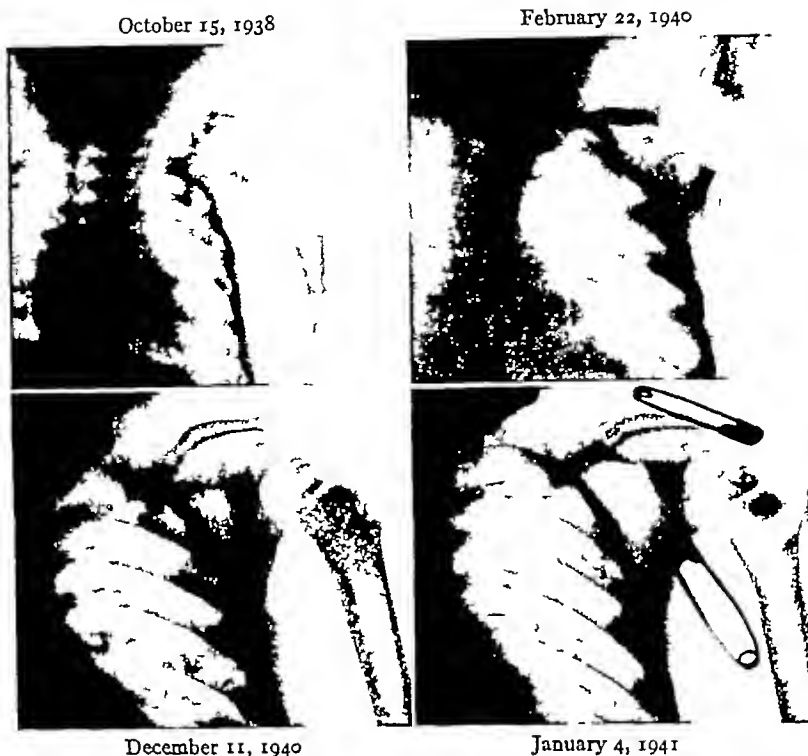


Fig 14 Case 12 Recurrent fracture of the clavicle in a 2 year old boy after an interval of 2 years and 2 months The first fracture occurred at birth and was observed to have healed without deformity in a study of the chest on February 22, 1940 The peculiar character of the second fracture line is well shown

1941, she went skiing and again injured the left forearm. X ray studies on the same day showed new fractures of both radius and ulna at the old fracture sites. There had apparently been complete healing at the old fracture sites with the formation of dense bone. The recent fracture lines had a different character and configuration than the first ones and resembled those seen in "brittle bones." Whereas the first fracture of the ulna was oblique the present one was transverse. No disalignment was demonstrable at this time except for the slight angulation of the ulnar fragments toward the radius with the former fracture well healed.

At an interview on March 10, 1941, she was seen to be a rather thin and pale girl weighing 46 kilograms with a height of 164 centimeters. There was an unusual degree of mobility at the joints but the sclerae were white and there was no deafness. Her mother described her appetite as very poor and she had always been smaller for her age than her two sisters. She disliked meat and could not eat eggs. There was a moderate intake of milk and fruit and small amounts of vegetables. The only fracture other than those described was one involving the right clavicle at the age of 7. No fractures had been experienced by the two sisters or either parent.

CASE 11 R DeT, C H F 8266 This boy was born of Italian parentage on October 5, 1931, and on December 1, 1940, while sledding placed his extended left arm against a tree to avoid hitting it and felt something snap. There was considerable deformity of the forearm and the x ray

examination a few hours later revealed fractures in the middle thirds of the radial and ulnar shafts (Fig 13). After several attempts at manipulation over a period of 6 days, the fragments were finally brought into a satisfactory position and alignment, as viewed in both planes. The history and physical examination at this time disclosed that he had been breast fed in infancy and had had no cod liver oil and very little orange juice. The tonsils were described as large and irregular and the teeth poor. There was no anemia—hemoglobin 13.7 grams/100 cubic centimeters—and the tuberculin and Kline tests were negative. The elbow and wrist joints were immobilized in plaster until February 4, 1941, and the arm was kept in a sling for another 2 weeks. The x ray examination of February 4, 1941, showed the alignment excellent in both planes with solid bony union occurring at both fracture sites. On March 11, 1941, the fracture was considered healed with a "good result."

The arm was used without pain or disability and neither the child nor his mother observed any difference in the size or alignment of the two arms. In March he played baseball pitching for a 4 man team which won the game. He also engaged in other sports, especially fighting, and his mother stated that he was always active as before. On April 8, 1941, while chasing a girl in a fight at school, he fell on his outstretched left arm and sustained another injury. X ray studies showed new fractures of the radius and ulna at the old fracture sites. The character and configuration of the fracture lines were quite different at this



December 9, 1940 February 4, 1941 April 8, 1941

Fig. 3 Case 1. Recurrent fractures of the left radius and ulna occurring in a 9-year-old boy after an interval of 4 months and 1 week. The healing of the first fracture was complete by ray films February 4, 1941 and by clinical examination, and free use of the part was regained. The different character of the new fracture lines to the old fracture sites is well shown.

next day showed transverse greenstick fractures of the middle thirds of the radial and ulnar shafts with slight palmar angulation at the fracture sites. After the manipulation plaster dressing was applied for 6 weeks. Satisfactory use of the part was obtained but for some time there was tenderness about the fracture sites and for a long time the part could ache during inclement weather. Even when recovery seemed complete her mother noted that she could tend to protect that arm. A second injury occurred on November 4, 1940, when she was struck in the posterior aspect of the lower part of the left upper arm. Swelling and ecchymosis appeared, and there was pain for a few days but the ray studies are negative and there is observed to be a normal appearance of the bone structure at the old fracture sites, with no deformity. The arm was carried in sling for 3 weeks, and good recovery was obtained.

On November 2, 1940, she fell on a tree while playing on the edge of a mud pit, again injuring the left forearm, and there was immediate severe pain causing her to cry for hours. The pain persisted and on December 3, 1940, she came to the clinic for ray studies. These showed soft periosteal shadow about the middle third of the radial shaft at the old fracture site and very slight disturbance in the bone structure, such as not present at the examination of November 6, 1940. Re-examination on December 28, 1940, showed some resolution and increased density of the periosteal deposits and the irregularity of the bone structure, as seen little more clearly so that there is no reasonable doubt that a second fracture of very limited subperiosteal type had occurred at the old fracture site.

At the interview of December 9, 1940, there was no complaint of pain and she exhibited free use of the arm,

although her mother said that there was sometimes pain at night requiring a hot water bottle. She had sustained no other fractures nor were there fractures at any of 6 siblings. Her appetite had been generally poor and she cared little for meat or vegetables. She was decidedly thinner and less robust than her healthy brothers and sisters. Her weight at this time was 36 kilograms for height of 135 centimeters. The ligaments about the joints showed more than the usual flexibility and the sclerae appeared thin with bluish cast. There was no deafness.

Case 9 McK. A little girl born on March 5, 1931, and living in comfortable circumstances, tripped over her rubber shoe running on playground at school and left on her extended right arm on November 20, 1940. She was referred to us a few hours later as private patient of Dr. Charles Kennedy and the ray examination showed greenstick fractures of the radius and ulna near the junction of their middle and distal thirds with sharp anterior and medial angulation to the fracture sites. Under ether anesthesia the normal alignment was restored, and plaster dressing was applied. Re-examination 14 days later showed the fragments in close end-to-end approximation with an excellent alignment in both planes. The immobilization was maintained for 4 weeks and then was discontinued temporarily for early physiotherapeutic exercises, extending over a period of 3 days, but the cast was discarded entirely. Convalescence was complicated at the point by a attack of chickenpox, but the normal use of the right arm was regained and there was no complaint or deformity of any kind.

On March 1, 1941, while roller skating she fell again on the right arm and sustained marked deformity as before. Refractures to the old fracture sites are demonstrated on the ray films but with slightly different character and configuration of the fracture lines. There was again marked angulation toward the radial and ulnar aspects.

At an interview on this date she was observed to be fairly well nourished blond girl of pleasing appearance and weighing 37 kilograms. Her height was 135 centimeters. The arms and legs are quite thin and there is more than the usual flexibility at the joints. Her mother described her as "poor eater" taking food very slowly and having no aversion to meat. She liked variety of vegetables, however, and drank three glasses of milk daily. The sclerae were white and there was no deafness. The patient had sustained no fractures of her teeth those described and none had been experienced by her mother or 4 sisters. Her father has been involved in accidents with fractures of the nose and the ankle.

Case 10 E. W. This girl, private patient of Dr. Darling of Pontiac, Michigan, was born on June 8, 1936. On June 27, 1940, while playing out of doors she jumped on a bench which tipped over and she was thrown to the ground on her outstretched left arm. Fractures of both bones of the forearm occurred, the ulnar fracture being quite oblique, with the end of the proximal fragment perforating the skin. X-ray studies (Fig. 10) on the same day showed the fractures. With angulation anteriorly and toward the radial side particularly at the ulnar fracture site.

The deformity as reduced by manipulation and plaster dressing was applied and kept on for 8 weeks. The arm was markedly trophic and remained thinner than the right one until the time of the second injury. There was no pain or other deformity, however, and the arm was used quite freely except for some slight limitation of pronation and supination. The fracture healed in the skin healed well and there were no signs of inflammation or infection.

She attended school during the autumn in good health and engaged in all of the usual activities. On February 9,

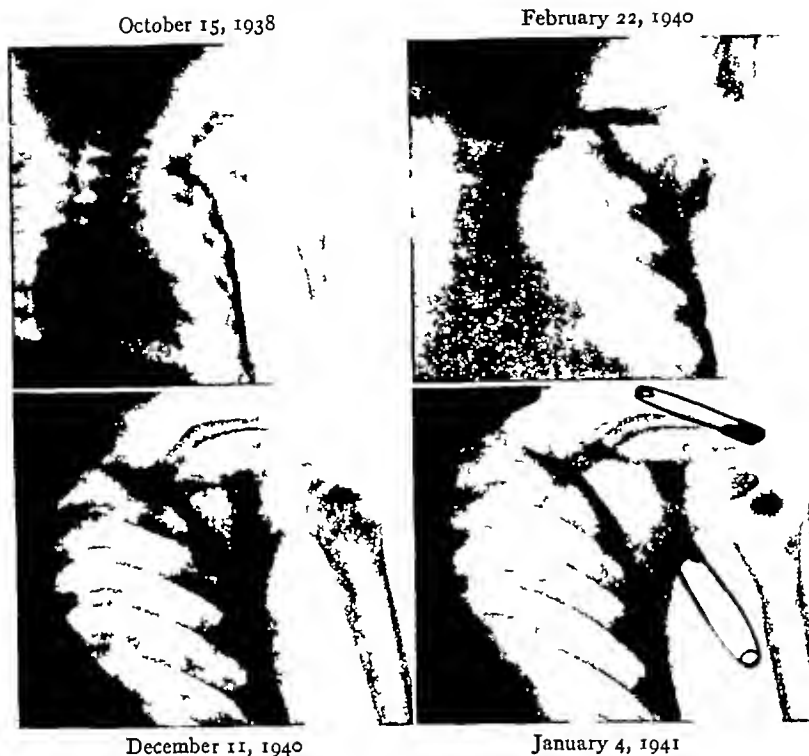


Fig 14 Case 12 Recurrent fracture of the clavicle in a 2 year old boy after an interval of 2 years and 2 months The first fracture occurred at birth and was observed to have healed without deformity in a study of the chest on February 22, 1940 The peculiar character of the second fracture line is well shown

1941, she went sking and again injured the left forearm. X ray studies on the same day showed new fractures of both radius and ulna at the old fracture sites. There had apparently been complete healing at the old fracture sites with the formation of dense bone. The recent fracture lines had a different character and configuration than the first ones and resembled those seen in "brittle bones." Whereas the first fracture of the ulna was oblique the present one was transverse. No disalignment was demonstrable at this time except for the slight angulation of the ulnar fragments toward the radius with the former fracture well healed.

At an interview on March 10, 1941, she was seen to be a rather thin and pale girl weighing 46 kilograms with a height of 164 centimeters. There was an unusual degree of mobility at the joints but the sclerae were white and there was no deafness. Her mother described her appetite as very poor and she had always been smaller for her age than her two sisters. She disliked meat and could not eat eggs. There was a moderate intake of milk and fruit and small amounts of vegetables. The only fracture other than those described was one involving the right clavicle at the age of 7. No fractures had been experienced by the two sisters or either parent.

CASE 11 R DeT, C H F 8266 This boy was born of Italian parentage on October 5, 1931, and on December 1, 1940, while sledding placed his extended left arm against a tree to avoid hitting it and felt something snap. There was considerable deformity of the forearm and the x-ray

examination a few hours later revealed fractures in the middle thirds of the radial and ulnar shafts (Fig 13). After several attempts at manipulation over a period of 6 days, the fragments were finally brought into a satisfactory position and alignment as viewed in both planes. The history and physical examination at this time disclosed that he had been breast fed in infancy and had had no cod liver oil and very little orange juice. The tonsils were described as large and irregular and the teeth poor. There was no anemia—hemoglobin 13.7 grams/100 cubic centimeters—and the tuberculin and Kline tests were negative. The elbow and wrist joints were immobilized in plaster until February 4, 1941, and the arm was kept in a sling for another 2 weeks. The x ray examination of February 4, 1941, showed the alignment excellent in both planes with solid bony union occurring at both fracture sites. On March 11, 1941, the fracture was considered healed with a "good result."

The arm was used without pain or disability and neither the child nor his mother observed any difference in the size or alignment of the two arms. In March he played baseball pitching for a 4 man team which won the game. He also engaged in other sports, especially fighting, and his mother stated that he was always active as before. On April 8, 1941, while chasing a girl in a fight at school, he fell on his outstretched left arm and sustained another injury. X-ray studies showed new fractures of the radius and ulna at the old fracture sites. The character and configuration of the fracture lines were quite different at this



March 3, 1930.



May 3, 1930



February 5, 31

Fig. 5. Case 3. Recurrent fracture of the clavicle occurring in a 4 year old girl after an interval of 3 year and 6 months. There was temporary deformity at the first

fracture site but healing at the time of examination was apparently complete and there was no evidence of disability present.

(time, however. The bone, although dense appeared to lack normal structure and the appearance of the fracture lines indicated an increased fragility.

At an interview on April 9, 31, he was seen to be an active child with thin, waxy extremities. There was little more than the usual flexibility of the ligaments about the joints and the sclerae were distinctly bluish, but there was no deafness. He weighed 26 kilograms and measured 37 centimeters in height. He had had no other fractures than those described and none was known in the parents or 4 other siblings. His mother described his appetite as good, with generous intake of eggs, vegetables, and meat, with fruit of some kind daily.

CASE 3. M. L., C. H. D 9432. This boy was born of Scottish parentage on October 1933, as one of a pair of twins. There was cephalic presentation and delivery

seemed to be uncomplicated, but weeks later deformity of the left clavicle was noted. The x-ray examination on October 5, 1933, showed fracture without displacement of the fragments in the middle third of the clavicle with large amount of callus at the fracture site. No treatment was advised, and in due course complete recovery occurred with free use of the arm and no signs of discomfort.

He suffered from frequent upper respiratory infections and was seen many times on this account in the Out Patient Department. On March 6, 1930, he fell about 3 feet, sustaining fracture of the right parietal bone. Recovery was complicated by meningitis for which bilateral mastoidectomy was performed. On February 2, 1930, in the course of an upper respiratory infection, an x-ray study was made of the chest which incidentally revealed complete healing with normal appearance of the bone



June 20, 1933.

November 24, 1939



June 20, 1933

November 24, 1939

Figs. 6, above, and 7 right. Case 14. Recurrent fracture in the proximal metaphyseal area of the right tibia in an 8 year old boy 6 years after the original fracture. Although the fracture sites appear to be identical the bone structure at the first fracture site has gone to form the cortex of the shaft and as the result of the growth of the bone has some distance distal to the second fracture site.

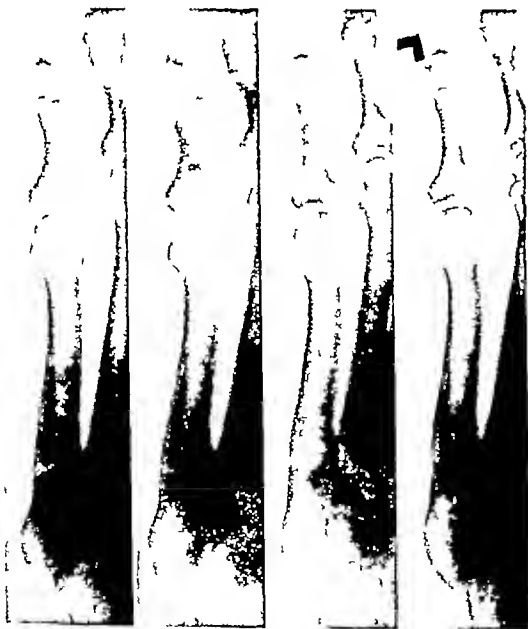
Fig. 7
(Legend in left column)

structure and no deformity at the old fracture site in the left clavicle

On December 11, 1940, he tripped while running with his twin brother and fell on his left shoulder with his arm beneath him. There was evident pain on lifting his left arm. An x ray examination on the same day revealed a simple transverse fracture line at the old fracture site. Any question as to the presence of a recent injury was answered by a re-examination on January 4, 1941, which showed a large amount of soft callus at the fracture site.

At an interview on this date the child was found to have a weight of 10 kilograms for a height of 83 centimeters. He seemed well nourished and his appetite was said to be excellent for a variety of foods. He had sustained no fractures other than those described and no fractures were recalled in the parents or in five siblings with the exception that one other child had sustained a fracture of the clavicle at birth. The sclerae were distinctly bluish and there was considerable flexibility of the ligaments but no sign of deafness.

CASE 13 B A, C H E 2202 This girl was born of Polish parentage on August 5, 1937, and was first seen at the Children's Hospital on March 22, 1939, following a fall on some steps which produced an injury to the right shoulder. The roentgen ray examination demonstrated a fracture of the clavicle near the junction of the proximal and middle thirds with the usual deformity. A dressing was applied for immobilization and maintained for 6 weeks. At the roentgen ray study of May 3, 1939, it was observed that osseous union was occurring with a large amount of



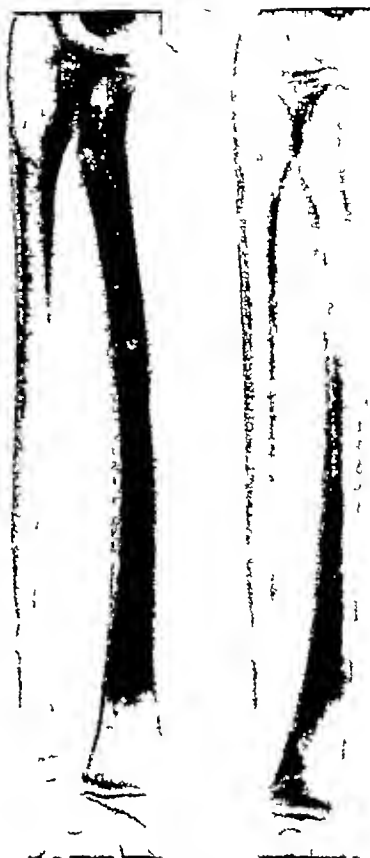
April 5, 1937

February 7, 1938

September 22, 1937

September 7, 1940

Fig 18 Case 15 Two recurrent fractures in the shaft of the fifth metatarsal bone of an obese, 18 year old boy, after intervals of about 5 months during which healing appeared complete. Each fracture was immediately preceded by an acute, severe trauma and the fracture lines have a slightly different character and configuration.



July 26, 1940

Fig 19 Case 16 Two views of the right forearm of a 6 year old boy showing a recent fracture of the radius near the junction of its proximal and middle thirds and the dense bone structure at the site of a fracture which had occurred 10 months before. The first fracture was in the distal third and cancellous portion of the diaphysis.

dense callus and with some overriding of the fragments, the distal end of the proximal fragment being displaced upward. After the dressing was removed, the child favored the right arm for a short period but she soon exhibited her normal right handedness, and there was no complaint or disability of any kind. The mother noted a lump at the fracture site but this disappeared in 1 or 2 months with no residual deformity. She experienced mild whooping cough in the spring of 1939 and chickenpox in the summer of 1940. She had suffered from eczema since birth and at 1 year of age was placed on a vegetable-poor diet for 6 months without benefit. There had been occasional colds and on December 24, 1939, she was hospitalized for nasopharyngitis, otitis media, and cervical adenitis.

On February 14, 1941, she fell from a couch and sustained a heavy blow to the right shoulder. Roentgen ray study revealed a new fracture without displacement or dislodgement of the fragments at the old fracture site. There was otherwise a normal appearance of the bone structure and the old fracture had apparently healed completely and without deformity.



March 3, 1930.



May 2, 1930.



February 5, 1931.

Fig. 5. Case 5. Recurrent fracture of the clavicle occurring in 4-year old girl after an interval of year and months. There was temporary deformity at the first

fracture site but healing at the time of examination was apparently complete and there was no evidence of disability present.

time, however. The bone, although dense, appeared to lack normal structure and the appearance of the fracture lines indicated an increased fragility.

At an interview on April 9, 1931, he was seen to be an active child with thin, bony extremities. There was little more than the usual flexibility of the ligaments about the joints and the sclerae were distinctly bluish, but there was no deafness. He weighed 26 kilograms and measured 87 centimeters in height. He had had no other fractures than those described and none was known in the parents or 4 other siblings. His mother described his appetite as good, with generous intake of eggs, vegetables, and meat, with fruit of some kind daily.

CASE 2. M. L. C. H. D. 943. This boy was born of Sicilian parentage on October 9, 1928, as one of a pair of twins. There was cephalic presentation and delivery

seemed to be uncomplicated, but weeks later deformity of the left clavicle was noted. The x-ray examination on October 3, 1928, showed a fracture without displacement of the fragments in the middle third of the clavicle with large amount of callus at the fracture site. No treatment was advised and in due course complete recovery occurred with free use of the arm and no sign of discomfort.

He suffered from frequent upper respiratory infections and was seen many times on this account in the Out Patient Department. On March 6, 1930, he fell about 3 feet, sustaining a fracture of the right parietal bone. Recovery was complicated by mastoiditis for which bilateral mastoidectomy was performed. On February 2, 1930, in the course of an upper respiratory infection, an x-ray study was made of the chest which incidentally revealed complete healing with normal appearance of the bone



June 20, 1933

November 24, 1930.

Figs. 6, above, and 7 right. Case 14. Recurrent fracture in the proximal metaphyseal area of the right tibia in an 8-year old boy 6 years after the original fracture. Although the fracture sites appear to be identical the bone structure at the first fracture site has gone to form the cortex of the shaft and as the result of the growth of the bone lies some distance distal to the second fracture site.



June 20, 1933

November 4, 1930.

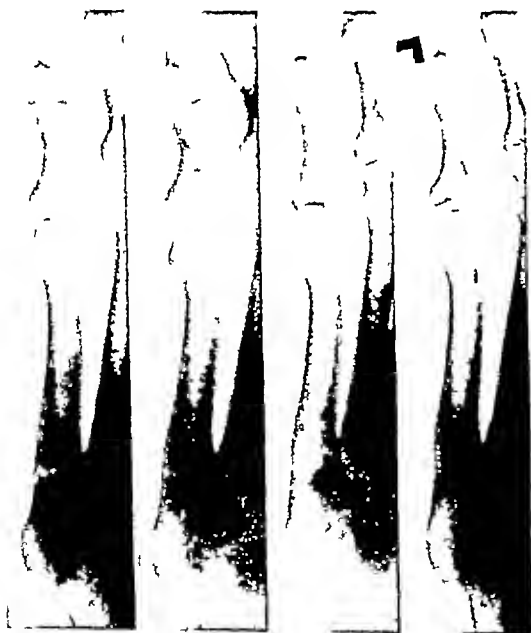
Fig. 7
(Legend: left column)

structure and no deformity at the old fracture site in the left clavicle

On December 11, 1940, he tripped while running with his twin brother and fell on his left shoulder with his arm beneath him. There was evident pain on lifting his left arm. An x ray examination on the same day revealed a simple transverse fracture line at the old fracture site. Any question as to the presence of a recent injury was answered by a re-examination on January 4, 1941, which showed a large amount of soft callus at the fracture site.

At an interview on this date the child was found to have a weight of 10 kilograms for a height of 83 centimeters. He seemed well nourished and his appetite was said to be excellent for a variety of foods. He had sustained no fractures other than those described and no fractures were recalled in the parents or in five siblings with the exception that one other child had sustained a fracture of the clavicle at birth. The sclerae were distinctly bluish and there was considerable flexibility of the ligaments but no sign of deafness.

CASE 13 B A, C H L 220. This girl was born of Polish parentage on August 5, 1937, and was first seen at the Children's Hospital on March 22, 1939, following a fall on some steps which produced an injury to the right shoulder. The roentgen ray examination demonstrated a fracture of the clavicle near the junction of the proximal and middle thirds with the usual deformity. A dressing was applied for immobilization and maintained for 6 weeks. At the roentgen ray study of May 3, 1939, it was observed that osseous union was occurring with a large amount of



April 5, 1937 February 7, 1938
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Fig 18 Case 15 Two recurrent fractures in the shaft of the fifth metatarsal bone of an obese, 18 year old boy, after intervals of about 5 months during which healing appeared complete. Each fracture was immediately preceded by an acute, severe trauma and the fracture lines have a slightly different character and configuration



July 26, 1940

Fig 19 Case 16 Two views of the right forearm of a 6 year old boy showing a recent fracture of the radius near the junction of its proximal and middle thirds and the dense bone structure at the site of a fracture which had occurred 10 months before. The first fracture was in the distal third and cancellous portion of the diaphysis

dense callus and with some overriding of the fragments, the distal end of the proximal fragment being displaced upward. After the dressing was removed, the child favored the right arm for a short period but she soon exhibited her normal right handedness, and there was no complaint or disability of any kind. The mother noted a lump at the fracture site but this disappeared in 1 or 2 months with no residual deformity. She experienced mild whooping cough in the spring of 1939 and chickenpox in the summer of 1940. She had suffered from eczema since birth and at 1 year of age was placed on a vegetable poor diet for 6 months without benefit. There had been occasional colds and on December 24, 1939, she was hospitalized for nasopharyngitis, otitis media, and cervical adenitis.

On February 14, 1941, she fell from a couch and sustained a heavy blow to the right shoulder. Roentgen ray study revealed a new fracture without displacement or disarrangement of the fragments at the old fracture site. There was otherwise a normal appearance of the bone structure and the old fracture had apparently healed completely and without deformity.



September 5, 1930.

Fig. 30. Case 7. T. view of the right forearm of an 8-year-old negro boy showing recent fractures in the middle thirds of the radius and ulna. The dense bone structure in the cancellous portion of the radius proximal to the distal epiphysis at the site of fracture which had occurred 3 months before.

At an interview at the time of the second fracture she was found to weigh 5.5 kilograms with a height of 95 centimeters and appeared well developed although her mother said she had poor appetite. She disliked meat but would eat milk, eggs, and vegetables. She was described as being very active with many falls and bruises but rarely any serious injury. She had sustained only the two fractures described, and there was no history of fracture in the parents or sister. The sclerae were considerably bluish but there was normal flexibility of the joints and no deafness was evident.

CASE 14. H. B. C. H. 890. A Jewish boy born on October 10, 1923, as seen in the Children's Hospital in 1923 and 1925 for various minor complaints including feeding problems. On June 8, 1925, he fell from a parked automobile and the right knee was noted to be tender. X-ray examination revealed a greenstick type injury of the tibia just beneath the proximal epiphyseal line (Fig. 6). There was no significant displacement or dislocation of the fragments and plaster cast as applied. Due to the mother's illness the child was not brought back for further care. After 6 weeks the cast fell off spontaneously. "Sores" and big blisters were seen on the leg and foot, and after many months of household remedies healing took place and normal use of the part was obtained. He became a very active child, indulging in violent games and sustaining many mild injuries. In August, 1927, he was treated for limited injury at the lower end of the left radius.

On November 24, 1929, while playing football, he fell striking his knee in the ground and again injured the right knee area. X-ray studies showed fracture lines at the proximal end of the tibial diaphysis in which he apparently normal bone structure. Healing took place in a satisfactory manner. He was without deformity or disability.

At an interview on November 30, 1930, he was observed to be well developed and measured boy weighing 35 kilograms and his height 135 centimeters. His mother stated, however, that he had been less active in the past and as "fussy" eater usually gave

thrust breakfasts and eating very little meat. The only other history of fracture in the family was in one brother who had sustained two fractures of the forearm. The patient's sclerae appeared normal and there was no deafness or hyperextensibility at the joints.

CASE 5. A. G. 85 years of age, private patient of Dr. J. O. Koppel. In April, 1917, while playing baseball, he turned his foot on a firm base. He was able to walk for 10 days but with much pain and on April 5, 1917, X-ray studies (Fig. 8) were made revealing fracture at the base of the fifth metatarsal bone. A plaster cast was applied for 3 weeks, and subsequently he was able to walk without disability.

In September, 1917, on jumping over a fence he felt something snap in the left foot. X-ray studies showed a new fracture in the fifth metatarsal bone and cast was applied for 4 weeks. There was satisfactory recovery and he was able to walk without pain or other disability.

One night in February 1918, he injured his left foot for the third time when he tripped over a wire in the dark. X-rays again showed the appearance of a new fracture and cast was applied for 4 weeks. Recovery was satisfactory as before.

When interviewed in September 1930, he was having no pain or difficulty in walking and roentgenograms revealed complete healing of the old fractures. He was observed to be a large, obese boy weighing 64 kilograms with a height of 135 centimeters. There was no deafness and the sclerae were blue but there was somewhat more than the usual mobility of the joints. He was not aware of having sustained any other fractures than those described in the left fifth metatarsal bone.

CASE 6. R. O. C. H. D. 650. This boy born on June 5, 1914, fell 3 or 4 feet to the ground from a porch on September 9, 1930, and sustained an injury to the right lower forearm. A diagnosis of fracture was made by the family physician. About an X-ray examination and splints were applied for 4 weeks. A good result was obtained with no further trouble until July 2, 1930, when he fell on his outstretched arm and hand while playing on a tree stump and again injured the right forearm. Pain persisted and a small area of ecchymosis appeared. An X-ray examination (Fig. 9) at the Children's Hospital 2 weeks after the injury revealed evidence of the old completely healed fracture at the lower end of the radial diaphysis and a more recent fracture of the radial shaft near the junction of the proximal and middle thirds. A plaster dressing was applied and retained for about 3 weeks, and the normal use of the arm was regained.

CASE 7. R. C. C. H. 70540. A colored boy born of epileptic parents on June 24, 1920, as seen in the Children's Hospital on many occasions for minor complaints. On June 20, 1930, he fell on his right hand and a greenstick fracture at the lower end of the radius, 10 centimeters proximal to the lower epiphyseal line, was demonstrated by X-ray. There was slight buckling of the cortex posteriorly but there was no important displacement or dislocation. Treatment consisted in immobilization in plaster for

number of weeks and a satisfactory result was obtained. On September 5, 1940, he fell on his outstretched hands while riding a bicycle and felt a sharp pain in the right forearm. X-ray studies showed complete healing at the old fracture site with new fractures in the shafts of the radius and ulna near the junction of their middle and distal thirds. After unsuccessful attempts to reduce the deformity by manipulation, an open operation was carried out with a satisfactory approximation of the fragments and a good final result.

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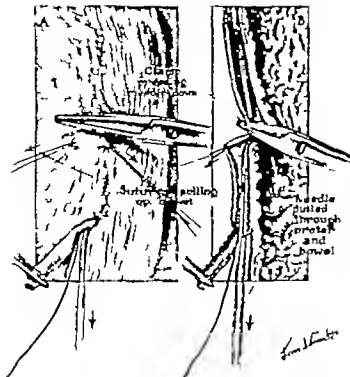


Fig. 4

Fig. 5. The needle emerging from the lower. It is grasped with clamp and the traction suture is pulled out of the eye of the needle.

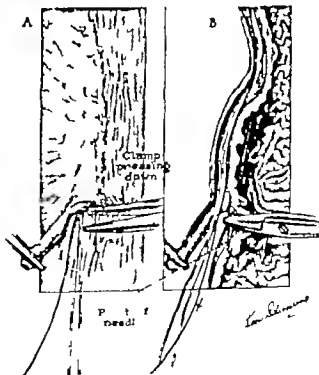


Fig. 5

IMPLANTATION OF URETERS INTO THE RECTOSIGMOID WITH A STUDY OF THE POSTOPERATIVE COURSE

EDGAR J. POHL, Ph D., M D., Baltimore, Maryland

DURING the past few years, numerous attempts have been made to improve upon old methods (5) and to devise new techniques (1, 3, 4, 6, 9) for the implantation of ureters into the rectosigmoid. Obviously, it is unphysiological to divert the urinary stream into the large bowel where the normal constituents of the urine will be acted upon by the ferments and bacteria of the intestinal tract. However, one is forced to form this outlet in certain instances of developmental anomalies of the bladder, or in cases in which the bladder must be removed because of malignancy or other disease.

The most important considerations in such an implantation are that the opening of the ureter into the bowel be adequate, pliable, and free of surrounding fibrosis, and that the ureter lie in the wall of the bowel for a distance before opening into the lumen of the intestine. Coffey demonstrated that this intramural segment acts as a check-valve to prevent the retrograde passage of material up the ureter when the bowel contracts. Since the intestinal contents are liquid after the implantation of the ureter and the delivery of urine into the intestine, it is particularly important that this valve function well so as to exclude the highly infectious material from the urinary tract. The most efficient check valve is ensured when healing between ureter and bowel occurs in a surgically clean bed, which is accomplished in a technique described by the author. The ureter has a fibrous tissue covering which is laid directly on the fibrous submucosa of the intestine. Infection in such an anatomical environment predisposes to excessive development of scar tissue, which will result in a stiff intramural tube, and will function poorly as a check valve against retrograde flow of fluid into the ureter. Furthermore, during the healing following the first stage, there is edema of the tissues involved, and they cannot respond to changes of pressure in the bowel. During this 10 day period it is important that the ureter shall not be open into the lumen

of the bowel, if retrograde passage of contaminated material up the ureter is not to occur and initiate a serious infection of the upper urinary tract. To have a properly functioning valve is considered of sufficient importance to justify an additional operative procedure when possible. The operation of implantation of the ureter is divided into two stages, in the first stage the ureter is embedded in the wall of the bowel without interruption or diversion of the urinary stream, and in the second stage the opening is made between the ureter and the bowel with diversion of the urinary stream into the intestine.

This unphysiological formation of a cloaca gives rise to a number of abnormalities, especially in the dog. Since this animal stands on all fours, his large bowel is in a practically horizontal position, and this position, coupled with the fact that in

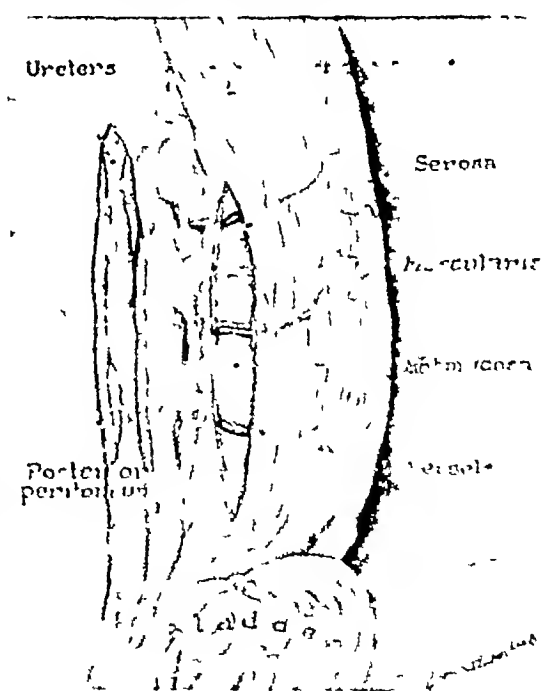


Fig. 1. First stage. Illustrates in a section of rectosigmoid down to submucosa with the preservation of the blood vessel, and shows the right ureter exposed and developed for implantation into the bed in the bowel.

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Reprint requests for this work should be sent to the Department of Surgery, Stanford University School of Medicine, San Francisco, California.

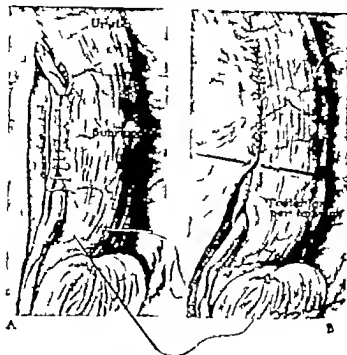


Fig. 2. First stage. a, Method by which the ureter is embedded into wall of bowel by means of continuous Lembert or Cushing suture of No. 3 chromic catgut. Serosum is left showing at both ends to avoid compression of the ureter. b, Manner in which cut edge of peritoneum is sutured over the implanted ureter. This obviates kinking of the ureter as it goes from its usual retroperitoneal location to its new bed in the wall of the rectosigmoid. Ten weeks are allowed for healing before the second stage of the operation is undertaken. Silk should not be used to close the intestinal bed because it frequently cuts through the underlying ureter even though interrupted sutures are employed.

the dog the large bowel has no well developed valves or folds but is rather straight and allows the fluid material resulting from the admixture with urine to flow upward to the ileocecal valve or even higher and gives rise to much reabsorption. This reabsorbed material appears to be rather toxic and results in a secondary anemia.

OPERATIVE PROCEDURES

In the course of this and previous studies numerous operative techniques have been used. When the single stage procedure is used in which the ureter is embedded in the wall of the bowel and the opening between ureter and bowel is made as advocated by Coffey, Mayo and Hinman (6) the survival rate is 5 to 10 per cent if both ureters are embedded at the same time. Death results from leakage, infection of the operative bed and peritonitis. In my hands, with the

technique advocated by Higgins, there was a mortality of approximately 25 per cent in the first stage from leakage and infection. The mortality in the two stage procedure previously described by the author and the modification here presented was less than 5 per cent in the experimental animal. These deaths were not due to leakage, infection or peritonitis, but were due to the small size of the structures resulting in technical difficulties and tearing of the ureter. Although the technique originally described by the author is entirely satisfactory for the experimental animal it cannot always be applied to the human being because the pressures of large tumors in the bladder or elsewhere pressing on the bowel may make it impossible to pass the proctoscope in the second stage. Although this technique is preferred whenever it is applicable, a second method has been developed for those cases in which the proctoscope cannot be inserted. The first stage is

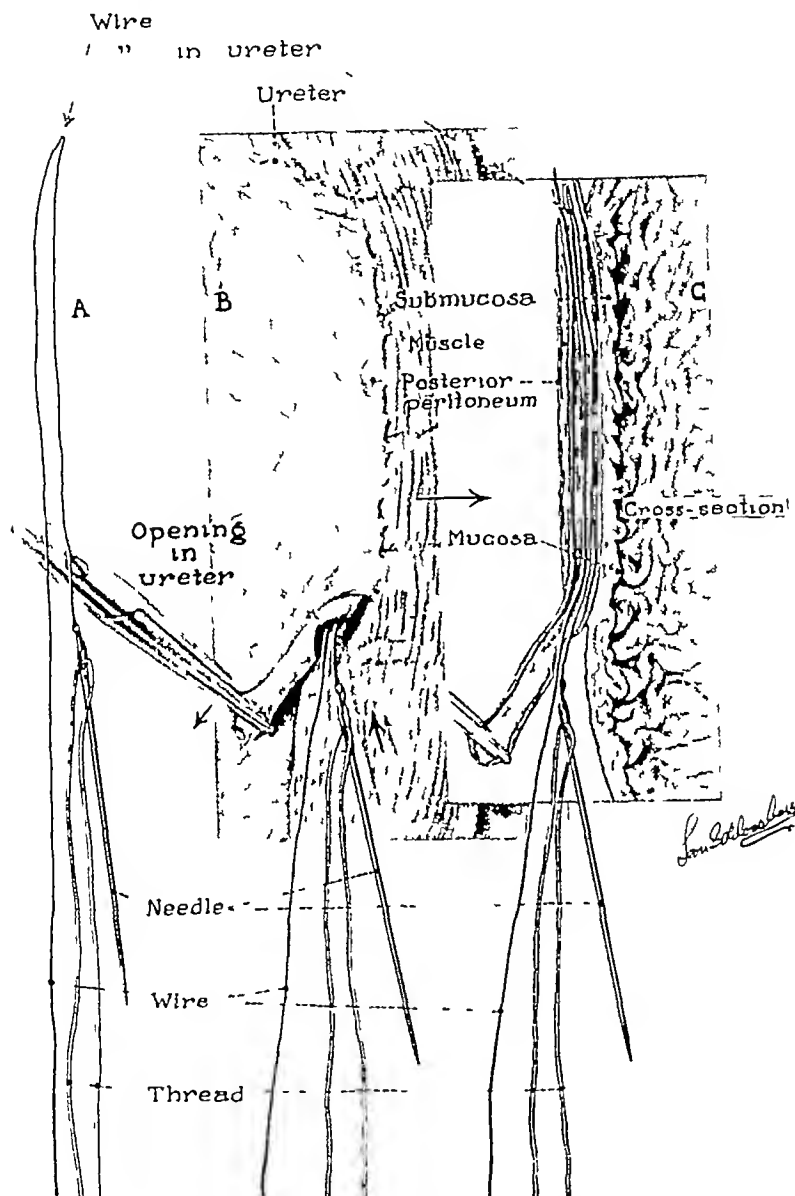


Fig 3 Second stage Two weeks have elapsed between first and second stages to permit aseptic healing of the ureter in its intramural location a An assembly of the cutting device consisting of a heavy darning needle mounted with a length of No 26 B & S gauge nichrome wire and a traction suture of fine braided silk This will serve as the cutting instrument to connect the lumina of ureter and bowel b, The cutting assembly being introduced into the ureter c, Same as b in cross section

essentially unchanged The second stage is not an entirely aseptic procedure, however, the most important healing of the ureter in its intramural bed has already occurred in a clean field If gross

soiling should occur at the second stage, the bladder should be removed at a later date The operation of ureteral transplantation on a debilitated human being is a considerable undertaking, and

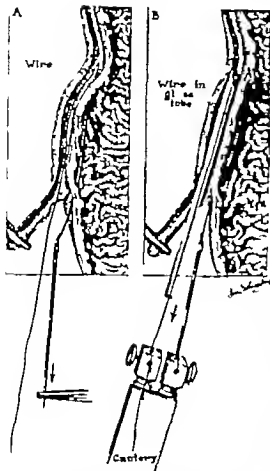


Fig. 6 A heavy rolled glass tube placed over one limb of the catheter to protect the ureter. A high cautery current is used in order that cutting will proceed rapidly as the instrument is withdrawn. The wire has been placed & cut slit about 5 centimeters long connecting the ureter and bowel.

one should be prepared to perform it in multiple stages and not to do too much at one time. The technical procedure can be readily followed in the illustrations.

THE UNPHYSIOLOGICAL STATE

Again it must be said that the dog is a poor experimental subject for ureterointestinal anastomosis. He walks on all fours, there are no valves in the large bowel, and he has a strong anal sphincter and a heavy well developed bowel musculature. The heavy bowel musculature causes a slight dilatation of the ureter above the implantation. This dilatation and obstruction is not sufficient to be demonstrable by intravenous



Fig. 7 The incision completed, the distal end of ureter is ligated, cut short and inverted into bowel. The opening in the bowel is ordinarily closed with single mattress suture. The area is covered with peritoneum as indicated.

urography. This change moreover, is not due to the ureters being subjected to the intraintestinal pressure because it develops even though the first stage only is done. The anthropological and anatomical arrangement of the dog is very excessive absorption of the urinary constituents from the bowel following ureterointestinal anastomosis. It is likely that some of the substances contained in the urine are altered by the bacterial flora and the fermenta in the bowel before they are reabsorbed. After transplantation of the ureters into the rectosigmoid the excrement from the bowel has a strong ammoniacal odor.

Although it has not been proved it is believed that the ammonia liberated by the urease acting on the urea of the urine excreted into the bowel is absorbed and acts as the toxic substance. A secondary anemia develops which does not seem to result from the increase in blood urea *per se*. The usual course of blood urea and hemoglobin levels are illustrated in Figure 8. Within 2 weeks after the first stage of the operation, nonprotein nitrogen blood level and the hemoglobin return to normal and would remain unchanged indefinitely. Following the second stage however when urine is being discharged into the bowel, there is a moderate and immediate rise in the nonprotein nitrogen level of the blood. After this immediate change the percentage of nonprotein nitrogen remains essentially constant, except for occasional

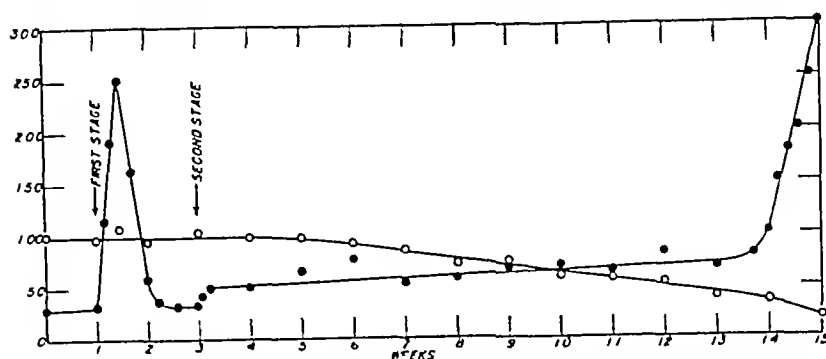


Fig 8 This chart illustrates the characteristic course of the nonprotein nitrogen (solid dots—mgm per cent) and hemoglobin levels (circles per cent) as observed in a series of 44 animals. Eventually all animals die following a sudden rise in nonprotein nitrogen and rapid fall in hemoglobin. Animals frequently survive for 6 to 8 months.

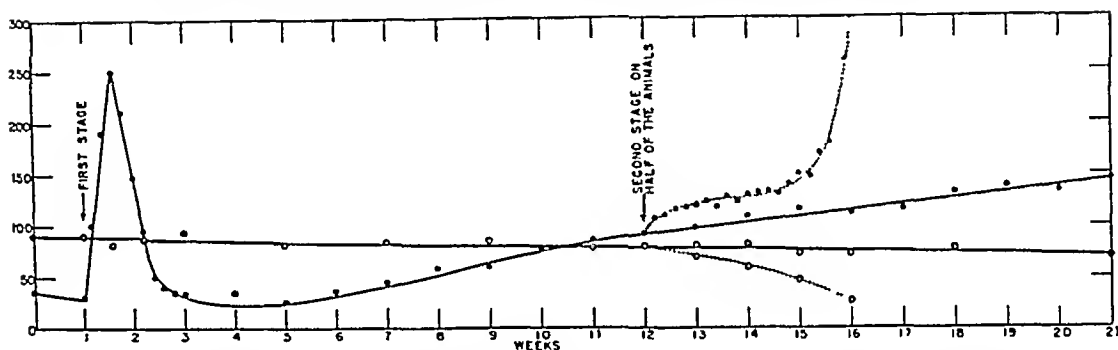


Fig 9 This chart illustrates the characteristic course of the nonprotein nitrogen (solid dots) and hemoglobin levels (circles) as observed in a series of 20 animals. Half of these animals were subjected to the first stage of the operation only, and the other half were operated upon twice as indicated, and their subsequent course is plotted by the dotted lines. The sudden increase in nonprotein nitrogen and the rapid decrease in hemoglobin occur only when the second

stage of the operation is done and urine is delivered into the large bowel. In all of these animals loose bands of cellophane or silk were placed around both ureters at the time of the first stage of the operation. These bands caused a gradual constriction of the ureters of the dogs. Animals have been known to tolerate for long periods of time a high nonprotein nitrogen blood level that is caused by simple obstruction.

periodic fluctuations, until the development of a rather severe secondary anemia. Following the establishment of an opening between the ureter and the bowel, the hemoglobin falls progressively and at a regular rate until it reaches 40 to 50 per cent. Up to this time the animal appears normal. There is then a sudden change, the animal refuses to eat, the rate of the hemoglobin fall increases, and the nonprotein nitrogen rises abruptly. Death, frequently accompanied by a *Bacillus coli* septicemia, occurs within a week. Necropsy shows the opening between ureter and bowel to be patent and soft, and the upper urinary tract is essentially normal both grossly and microscopically. Apparently the fall in hemoglobin is not dependent upon the nonprotein nitrogen level of the blood. In a group of 20 animals bands of cellophane or silk were, at the time of the first operative stage,

placed loosely around both ureters proximal to the implant. These animals show the usual immediate elevation of blood urea, with return to normal for a period of weeks, and then, with the gradual development of fibrosis in the region of the bands and constriction of the ureters, the nonprotein nitrogen of the blood rises slowly to high levels. During this time there is but a slight drop in hemoglobin. If on alternate animals, however, the second stage of the operation to deliver urine into the bowel is performed, the courses followed by the two groups are entirely different. From the difference in the blood pictures of the two groups, as illustrated in Figure 9 it appears that the nonprotein nitrogen blood level is not responsible for the anemia, but rather that substances are being absorbed from the bowel which react to cause this and other changes.

Whether this intoxication is due to the absorption of ammonia from the bowel for resynthesis into urea by the liver which in turn is re-excreted by the kidney to establish a vicious cycle has not been proved but is postulated as a possible reasonable explanation of the anemia and the death of the animals.

EVALUATION

The marked rise in blood urea following the bilateral embedding of ureters in the first stage demonstrates conclusively that both ureters should not be embedded simultaneously in a debilitated person with a high initial blood urea. If preoperative intravenous urography shows the ureters to be greatly dilated it must be appreciated that these enlarged structures cannot be successfully buried in the wall of the bowel. Under these circumstances it is well to consider nephrostomy as recommended by Cabot and to allow sufficient time for the ureters to decrease in size and for the kidney function to improve. Nephrostomy followed by the simultaneous embedding of both ureters is a simpler safer and more satisfactory procedure than dealing with the ureters singly. The use of ureteral catheters during this period has been suggested, but this may be impossible mechanically and catheters are poorly tolerated in the presence of the infection frequently found in urinary stasis.

In view of the rise of blood urea and the fall of hemoglobin and their apparent association with the reabsorption of toxic products following the delivery of urine into the rectosigmoid, it is suggested that the patient be placed in the semi-Fowler position as soon as practical after operation that a small rectal tube be inserted just

beyond the sphincter ani and that he be encouraged to evacuate the bowel frequently. Jewett induced the anal sphincter of dogs to facilitate emptying the bowel.

Frequent hemoglobin determinations should be done. While in bed, the patient should assume the semi-Fowler position and be awakened once at night to empty the bowel. Mild cathartics may be indicated.

It cannot be repeated too frequently that the healing following embedding of the ureter in the wall of the bowel should occur in the absence of infection in order to ensure a patent orifice and a soft, readily compressed intramural bed for the ureter.

SUMMARY

1. An alternative procedure is presented for the second stage of the operation for ureterointestinal anastomosis.

2. The unphysiological state created by the formation of an abnormal cloaca is discussed.

3. A secondary anemia following ureterointestinal anastomosis is reported.

4. The cause of late death of the experimental animals is considered.

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INTERNAL WIRE FIXATION FOR FRACTURES OF JAW

Preliminary Report

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IN some fractures of the lower jaw, in which interdental wiring cannot be done, a wire—of the Kirschner type—drilled across the fracture line may be an easy and satisfactory method of treatment

The indication for this internal fixation may be present when the opportune early time for interdental fixation has passed and the fragments have become displaced, with compounding into the mouth, infection, and local sloughing. It also may

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be considered in edentulous jaws, when there is much comminution and accompanying injury, as in gunshot and war injuries, when many teeth have been loosened or broken, in displaced symphysis fractures, and in fractures at the angle in which the posterior fragment is pulled out and up into the upper buccal fornix by the closing muscles (Fig 3). This last deformity is one of the worst to contend with, and, if left uncorrected, may result in non-union of the fragments. It may also prove to be of value in certain separations of the upper jaw.



Fig 1. Bad comminution at symphysis with only small points of bone in contact, left condyle and many teeth broken. Fixation at symphysis with one internal wire and a

second plane of fixation obtained with an anterior wire arch. Jaws wired together because of the condyle fracture opened after 4 weeks with internal wire still in place.

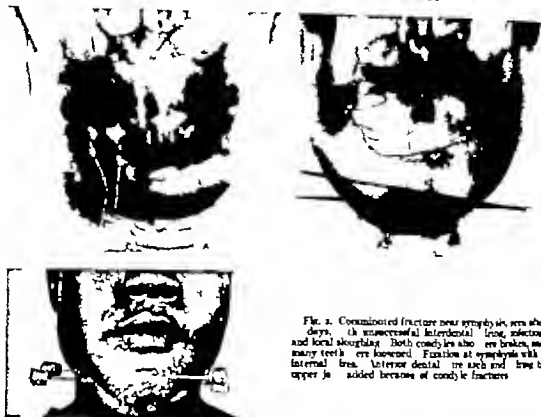


Fig. 3. Comminuted fracture near symphysis, seen after days. (1) unsuccessful interdental lining, infection, and local sloughing. Both condyles also are broken, and many teeth are loosened. Fixation at symphysis with internal bra. Anterior dental arch and bra to upper jaw added because of condyle fractures.

The internal wire will insure fixation in one plane—that is, the fragments cannot slip up or down past each other. However they might rotate in or out, or they might pull apart and, therefore *the addition of an anterior wire dental arch* will give a second plane of fixation that will prevent rotation and will jam the fragments in impaction so that separation will not occur. If there is a condyle fracture to deal with also, or if normal occlusion cannot be maintained then there can be the *further addition of interdental fixation to the upper jaw*.

Multiple internal wires can be used for multiple fractures, or to give the second plane of fixation if desirable.

Isolation of the nerve canal is advisable even though the nerve may have been cut in two by displacement of the fragments. The same is true of any good teeth and this can usually be done by staying below the canal. When a second wire is placed above the lower one there is more chance of damage of the nerve and teeth.

An electric power drill is practically necessary as the hand drill may not give enough speed for easy penetration of the bone. Regular Kirschner

wires may be used, but stainless steel wires, recommended by Dr. C. H. Crego in leg lengthening are cheaper and can be obtained in suitable lengths of thickness from .05 inch to .08 inch, a three-sided point being put on them. Bicycle and velocipede spokes also have been used by Dr. Crego.

A further modification is to cut threads all the way along an .08-inch wire with a 2-56 die which is a bicycle spoke threader and, after it has been drilled into position, screw regular bicycle spoke nipples or small nuts down against the bone to hold the fragments together. This threaded wire itself may give sufficient tightness without the nipples to prevent separation and is applicable to edentulous patients or any time the dental arch cannot be used (Fig. 4).

OPERATION

Local or deep block anesthesia is usually employed. The fragments are aligned with the hands,

This wire is 18-8 stainless steel. The smallest size to give the necessary stiffness is preferable.

I have been suggested by Dr. J. A. Brown that the threaded wire might be cut and have fixation against the bone secured, but low cylinder could be slipped over an unthreaded wire down against the bone and held with set screw put in the end of



Fig 3 Fracture at angle with elevation of posterior fragment and loss of mandibular nerve sensation. Fixation with single internal wire put in from behind and below the nerve canal. Avoidance of open reduction or elastic traction reduction of posterior fragment. Interdental wiring was done because of second fracture in body. At right, mouth open, with wire in place.



or an open reduction may be necessary, an elevator being used between the fragments. It is important that reduction be accurate, as only slight adjustment is possible after the wire is in.

A puncture incision is made to get the wire in against the bone, and the wire and drill are lined up accurately. Then, perhaps most important of all, the fragments have to be held in accurate position with the hands while the wire is drilled into place. (Little mention need be made of the necessity of care with the drill and wire, and for avoidance of injury to the hands that are holding the fragments.) The wire usually is drilled on through the bone and a small opening is made to let it through the skin on other side. Secondary internal wires may be needed occasionally (Fig 2).

The anterior arch wire is applied by putting No. 26 stainless steel wires on posterior teeth on each side, twisting the strands tightly for 2 inches, then twisting them together in midline and holding them with individual No. 28 wires around separate teeth. Any other type of arch appliance may be used, but this one requires no added equipment and is usually satisfactory.

This is the wire that should suffice for the second and final plane of fixation and should impact the fragments together over the internal wire (Figs 1, 2, and 4).

Interdental fixation is done as mentioned, if there is some final adjustment of occlusion to be secured or if the condyles also have been fractured. The jaws may be fastened directly together or by any effective method of elastic traction.

In edentulous jaws, when dental plates wired or bandaged in place with the mouth closed will not suffice, a single internal wire or a threaded one as shown in Figure 4 may be effective as the jaws are usually small from atrophy anyway. This plan for edentulous jaws seems much less trouble for the patient and surgeon than attempting any rigid fixation within the mouth with screws down into the bone and nerve canal.

Sulfanilamide is used locally in all open wounds and right in the fracture line if it has been separated widely enough to admit the powder. Wounds of the mouth, jaw, and neck, with their marked tendency to infection, make a field of great importance for the use of this drug.



Fig. 4. 8-8 stainless steel 1/2 in. of lock threaded with 2-50 die-cutter such as bicycle spoke-threader and with regular bicycle spoke nipples screwed on. (Equipment, courtesy Dr. Crego). In the patient shown, the fracture is

Pressure dressings of soft cotton mechanics waste are applied to give support to the soft tissues and prevent, as far as possible, hematoma, hemorrhage, and swelling, and also to lend further support to the bone fragments.

The jaw seems solid immediately and the patient experiences the usual comfort of a set fracture. The ends of the wire are covered and the patients do not object much to discomfort. In some instances, the wires may be cut short enough to be covered by the skin, but it is probable that they all should be removed finally. Just one or two days are required in the hospital, and some patients can open the jaws and take soft foods almost immediately.

The removal of the wires can be done easily after 3 to 5 weeks, depending upon the progress. There may be some irritation around the wires but no serious osteomyelitis should develop.

held with an internal threaded 1/2 in. and one nipple. The mouth could be opened easily after the operation, and soft food was taken. Anterior arch was put on to hold separate loose fragment.

This plan was thought to be new but articles on the subject were found by Ipsen and Sobye in Denmark and Meade in Ireland and these men seem to have been the only ones to have reported it.

In the voluminous literature from the last war and since then, there has been a multiplicity of dental splints, often with emphasis on some contrivance of little fundamental bearing. If this simple direct method of internal wire fixation by drilling wire across the fragments will help to rid the use of complicated dental splints, overhead plaster-cap traction for elevated posterior fragments, and wide open reductions, it will be worthwhile.

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REACTION OF BONE TO METALS

II Lack of Correlation with Electrical Potentials

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EXPERIMENTS in which as many as four different kinds of metals or alloys were implanted into the femurs of cats were reported in an earlier paper (Bothe, Beaton and Davenport, 1940). Differences in electrical potentials between a number of the implants were taken *in vivo* after a postoperative survival period of about 7 months and the reaction of the bone to the various metals was studied. The correlation between electrical potentials and bone reaction was not good, and in view of the emphasis that has been given to electrolysis, it was decided to make another series of implantation experiments to test the effect of electromotive force more accurately.

Some of the more pertinent references to experimental and clinical experiences with bone reactions to metals were cited in the preceding paper, and two more which deal with electrical phenomena can be mentioned here.

Berti-Riboli (1938) measured potentials between bone and metals at three different time intervals after applying plates to the long bones of rabbits and dogs. The method of making the measurement of the electromotive force between the bone and the plate is not made clear, but the difference of potential was found to diminish with time. Copper, aluminum, stainless steel (3 kinds), duraluminum and 20 carat gold were used, and there was a difference in the rate of diminution of potential for each metal. A hypothesis was proposed that the rate of diminution was directly proportional to the toxicity of the metal.

Hudack (1940) reported on the use of high chromium, low nickel stainless steel, and emphasized the necessity of polishing and of treating alloys with nitric acid to minimize the presence of foci for electrolytic corrosion.

It has seemed to us that too much emphasis has been placed on electrical effects and too little on the more general properties of the solubility of metals in body fluids and the reaction of tissues to the dissolution products. In order to test the influence of differences in electrical potential in contrast with characteristic properties of individual metals, we have implanted two instead of

four metals into each bone and have attempted to correlate reactions with electromotive force differences.

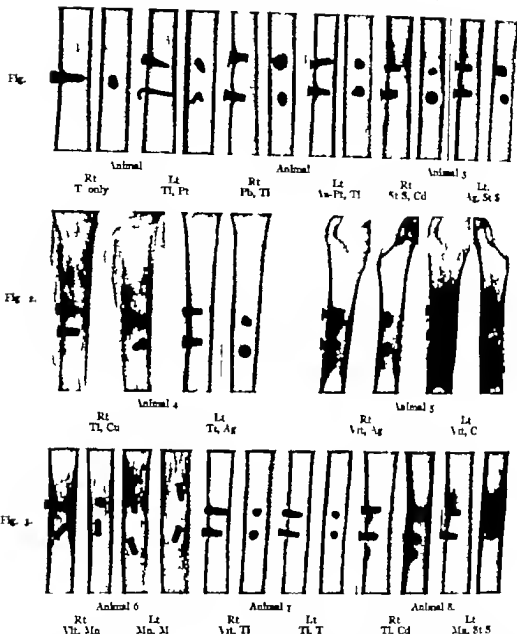
Experimental. One male and 16 female cats were used. Two implants, usually of different metals were made into each femur. The technique of making the implantation was the same as that used in the previous experiments. All 17 animals survived the experimental period, and were sacrificed at intervals between 186 and 329 days. Electrical potentials between the two implants, and also the potential from a copper electrode in the adjacent muscle to each implant, were measured while the animal was under anesthesia just prior to sacrifice. A few of the implants had become buried in the bone and potentials on them were not secured, and one had sloughed into adjacent soft tissue.

In arranging the pairs of metals, the object was to secure (1) pairs with rather large potential differences, (2) pairs with medium potential differences, and (3) pairs with little or no potential differences. The results are listed in Table I. A critical examination of the potential differences shows that they are not reproducible from animal to animal with the degree of accuracy that might be desired, but that the order of magnitude permits them to be grouped into low, medium, and high. The potentials have been correlated with the amount of bone reaction, and a recapitulation of the findings made in Table II.

RESULTS

It is seen in Table II that 7 of the metals or alloys reacted in the direction of their electrical differences while 10 did not. This is interpreted to mean that there is no direct correlation between a condition which predisposes to electrolysis and one which does not. Reactions occurred in the regions immediately surrounding the offending metal. However, had metallic ions been carried from one metal to the other as a result of electrical effects, we would expect to see reactions about both implants. In only one femur (cat 4, Fig. 2) which received titanium and copper, was the reaction so extensive that it spread far enough to make uncertain which one of the pair was the offending metal. Comparing this femur with the

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left one makes it evident that copper and not titanium is toxic, since titanium was not reactive when paired with silver or when used alone (cats 1 and 7). In the left femur of cat 5 the difference in potential between copper and vitallium was zero, yet a vigorous reaction occurred. From other potential measurements it can be deduced that the difference between copper and titanium is not

over 20 millivolts and would not be enough to account for the extensive reaction of the right femur of cat 4.

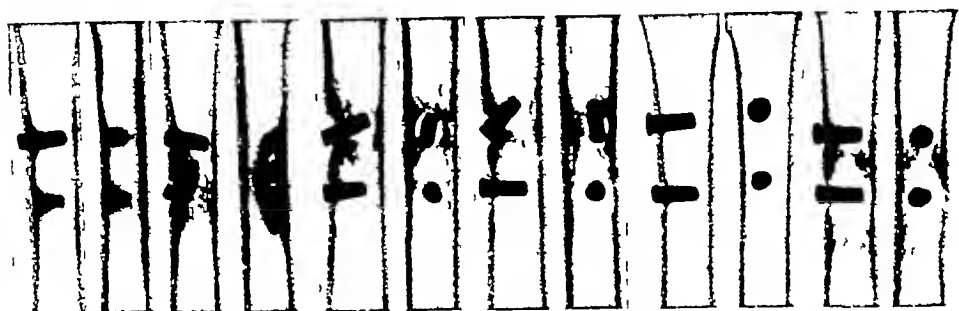
Another example of an unfavorable reaction with low potentials is seen in the case of nickel implants of cat 3, Figure 5. The potential difference between nickel and chromium on the right side was 20 millivolts, whereas on the left

Fig 4



Animal 9 Animal 10 Animal 11
 Rt Lt Rt Lt Rt Lt
 Ti, Mn Ag, Mn Vit, Mn St S, Mn Ti, Mg Pb, Mn*

Fig 5



Animal 12 Animal 13 Animal 14
 Rt Lt Rt Lt Rt Lt
 Mo, Al Mo, Mn Ti Ni, Cr Ni, Co W, Fe Ti W, Co

Fig 6



Animal 15 Animal 16 Animal 17
 Rt Lt Rt Lt Rt Lt
 Cr Mn, W Ti, Be† Mo, Be† Mo, Al Cr, Cr Mn Fe-Ti, Mn-Ti

Figs 1 to 6 Roentgenographic positive prints of cat femurs cleaned and photographed after a postoperative survival period of 186 to 329 days. Side and end views of

*This implant had sloughed out of the bone and was encapsulated in the adjacent soft tissue

the metallic implants are shown in the right and left femur. The proximal end of the bones is at the top of the figures, and the metals used are listed from proximal to distal.

†Beryllium (atomic weight 9.02) is more transparent to x rays than is bone. Both of these implants are in situ.

between nickel and cobalt it was 130. The reaction is essentially the same on both sides and is characterized by a marked erosion without cortical proliferation. Chromium has remained inert on the right while cobalt has caused some erosion on the left.

An example of moderate potential difference between lead and titanium with little reaction is seen in the right femur of cat 12 with an electromotive force of 260 millivolts. There is evidence of only a slight cortical reaction with bone grown over about half of the exposed surface of the lead im-

TABLE I.—DATA ON REACTIONS OF FEMURS OF CATS TO PAIRS OF METALLIC IMPLANTS

Cat no and post-operative period (days)	Side and metals implanted	F M F between metals (mm.)	Type of reaction
139	Rt Ti only		Marked cortical thickening
	Li Ti, Pt	70	Slight cortical thickening
21	Rt Pb, T	100	Cortical thickening
	Li Au-Pt, Ti		Marked surface erosion about the Au-Pt alloy
203	Rt Sn S, Cd	100	Modest surface reaction about Cd, but none
	Li Ag, Sn S	100	Slight increase of medullary density Ag
17	Rt T, C	T covered, no of bone*	Absent reaction with local erosion about C
	Li Ti, Ag	Not taken	Some callus about Ag
19	Rt Li, Ag	70	Increased density Ag
	Li Sn, Cu		Callus and local erosion, Cu
210	Rt Sn, Mn	Mn in medullary cavity	Increased density
	Li Mn, Mn		Cortex intact
20	Rt V, T		Slight cortical thickening
	Li T, Ti		Slight cortical thickening
208	Rt Ti, Cd	100+	Medullary condensation, Cd
	Li Mn, Sn S	Mn covered 100 or more*	Callus and slight local erosion about M
204	Rt Ti, Mn	Mn covered	Callus, and increased medullary density Mn
	Li Ag, M	100+	Ag, erosion pronounced Mn, proliferative pronounced
39	Rt Vn, Mn	100+	
	Li Sn S, Mn	100+	Marked proliferation about Mn
	Rt T, M	100+	Mg, not all absorbed, slight increase in density
201	Li Pb, Mn	M dissolved out of bone	Pb partly covered
46	Rt Mn, Al	100+	Cortical thickening about both
	Li Mn, Mn-T	Not taken	Mn covered by callus produced by Mn-T alloy
26	Rt V, Cr	70	V marked erosion about cortical proliferation
	Li Vn, Cu	70	V shows some medullary thickening, Cu, reaction with cortical thickening
12, 130	Rt W, Fe-T	70	W, begins Fe-T cortical thickening
	Li C	70	C shows local reaction with thickening on and near distal end
	Rt Cr Mn	100+	C Mn, slight cortical change
	Li T, Sn	100	Practically no reaction
70	Rt Mn, Be	100+	Slight cortical thickening
	Li M, Al	100+	Slight cortical thickening

TABLE I.—DATA ON REACTIONS OF FEMURS OF CATS TO PAIRS OF METALLIC IMPLANT—Continued

Cat no and post-operative period (days)	Side and metals implanted	F M F between metals (mm.)	Type of reaction
17, 14	Rt C, Cr M	100+	Some cortical and ulnar reaction, Cr Mn
	Li Fe-T, M T	Not taken	Mn-T increased ulnar reaction and bone callus

* Estimated from other determinations on similar couples.

plant. On the left side of the same cat the difference between titanium and a gold-platinum alloy was zero and there is practically no bone reaction, but the alloy pin remained loose as if the bone were voiding it. This is in contrast with the growing into contact with the lead.

Another instructive example of the lack of direct correlation between potential and reaction comes from the comparison of the reactions of manganese and cadmium. When either of these was implanted adjacent to a nonreactive pin of vitalium, stainless steel, or titanium, a high potential difference resulted. Couples containing manganese gave vigorous reactions but those con-

TABLE II.—POTENTIALS AND TYPES OF REACTION OF BONE TO METALS

Potentials			Reactions		
230 mv or more	70 to 200 mv	100 mv or less	Marked	Moderate	Slight
Al	Ag	C	(Fusion)	Ag	
Be	Cu		Cu	Cd	Be
Cd	C	Pt	N	M	Cr
Mg	Mn	Sn S	(Fusion)		Mn
M	Pb	Ti			Pb
		V	Cu		Pt
			M		Sn S
					Ti

Correlation of potentials and reactions. High potential and marked reactions, Mn, moderate potential and moderate reactions, Ag, low potential and slight reactions, Pt, M, V, not correlating with the voltage alone. Al, Be, Cd, Cr, Cu, Fe, Li, M, Mn, Ni, and Pb.

A copper electrode as adjacent anode as used arbitrarily as zero point of reference because most of the couples in the bone contained one implant which gave very low potential with copper. Reactions are classified according to gross appearance and x-ray photographs.

training cadmium gave very mild ones (cats 3, 6, 8, 9, and 10), and the reactions are centered around the reactive metal and not around the pair forming the electrolytic couple. Beryllium couples with high potentials (cats 15 and 16) show even less reaction than those containing cadmium.

In one instance (cat 6) manganese implants became completely intramedullary and the cortex healed over them. The titanium pin on the right side remained in place. One may imagine that the formation of insoluble manganese soaps from fat in marrow cavity on surface of the pins tended to inactivate them and permitted healing of cortex.

The activity of manganese was greatly reduced when alloyed with chromium (manganese 70 chromium, 30 parts) but the potential between the alloy and a copper electrode in adjacent muscle was similar to the unalloyed manganese. A manganese titanium alloy (manganese 65 titanium 35 parts), on the other hand reacted similarly to unalloyed manganese. This illustrates the well known property of chromium to suppress corrosion of metals with which it is alloyed.

The present study together with the observations made on the preceding series, throws some light on the behavior of bone toward metals as determined by their solubility. Evaluation of every metal individually is necessary. For example magnesium is very soluble but not particularly toxic while copper is much less soluble but highly toxic. Chromium would be very toxic if it were soluble, since chromium salts are very toxic to all living tissues, but the metal caused no reaction. Beryllium caused little reaction presumably by reason of its insolubility but beryllium salts are known to cause bone lesions similar to rickets when taken by mouth. Lead shows no toxicity is judged by the tendency of the cortex to cover it, yet lead salts are toxic.

Tantalum was not used in this series, but the report of Burke indicates that this metal is quite inert in both bone and soft tissues and has ideal physical properties. The fact that tungsten was inert in our experiments and that it is closely related to tantalum in the atomic series of the elements is of some academic interest.

PRACTICAL CONSIDERATIONS

The possibility of using powdered, sterilized metallic manganese to stimulate callus formation in

nonunion of fractures is suggested by the way bone reacts to this metal. It appears to be largely inactivated in the medullary fat, as shown by the femurs in which it became intramedullary and the cortex healed over it with scarcely a trace of the original holes. The powdered or finely granulated metal might be sprinkled on the exposed nonunited ends of a bone during an open operation, or it is conceivable that it could be injected without an operation in a suspension of an absorbable medium.

Differences of electrical potentials in themselves do not cause unfavorable bone reaction hence it seems reasonable to conclude that any alloy which might be made of metals with which bone reacted favorably individually would be tolerated well in alloy. This postulate should be of value to the metallurgist interested in the manufacture of prosthetic materials.

SUMMARY AND CONCLUSIONS

Two implants of dissimilar metals were paired in such a way that varying degrees of electrical potential were obtained, and allowed to remain 6 to 11 months in femurs of cats. Bone reactions were not closely correlated with the magnitude of potential differences, but remained characteristic for a given metal or alloy. Electrolysis is not the primary cause of unfavorable bone reactions. The primary causes are determined by physical and chemical properties of the metal itself. Solubility and the degree of toxicity of the dissolution products appear to be the chief factors. If electrical potentials play no part in inciting reaction it seems safe to assume that the unfavorable reactions seen in alloys are due to the presence of toxic metals (such as nickel, copper, or manganese) in them. Alloys which consist of nontoxic metals should be nontoxic regardless of potential differences of their components. Theoretically, vitallium comes nearer to meeting this requirement than stainless steel, but tantalum may prove to be the metal of choice when sufficient data on it have been accumulated.

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THE MANAGEMENT OF ACUTE EMBOLIC OCCLUSION OF THE ARTERIES TO THE EXTREMITIES

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WHEN an artery in an extremity becomes acutely obstructed by an embolus, a two-fold therapeutic problem presents itself. The first is in the nature of an emergency. It is the necessity of immediately restoring sufficient circulation to preserve the viability of the limb. The second is predicated on the successful accomplishment of the first. It is to promote therapeutically the growth of a collateral circulation so that the functional capacity of the limb as well as its viability will be preserved. Both are accomplished by increasing the volume rate of blood flow through the available collateral circulation.

For practical therapeutic purposes, any method designed to augment the quantity of blood flowing through a collateral arterial network must exert its effect by diminishing the peripheral resistance to blood flow through a dilatation of the arteriolar capillary bed into which the collateral vessels ultimately empty. Since ischemic tissue is saturated with vasodilating substances, it should be expected that such an increase in the flow of blood through collateral channels would automatically follow the acute occlusion of a principal artery. As a matter of fact, cases of acute embolic occlusion are not infrequently seen which open and develop an effective collateral circulation without any therapeutic assistance. Many more would respond in a similar manner were it not for the fact that when an embolus suddenly occludes a peripheral artery the arterial bed in that extremity and sometimes in the opposite extremity as well as thrown to a greater or lesser degree of spasm. I have seen instances in which a minute embolus lodged in the periphery of a leg has given rise to bilateral vasospasm of such magnitude that an organic occlusion of the bifurcation of the abdominal aorta was simulated. A case in point follows:

A K., white female aged 37 years, came under observation December 1, 1940. For years she had suffered from rheumatic carditis with fibrillation for many years, but as well controlled. While convalescing from an elbow operation, she suddenly experienced an acute severe pain in her right leg and foot accompanied by sensations of coldness and numbness.

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About 30 minutes later similar symptoms appeared in the right foot and leg.

The patient appeared to be acutely ill and in considerable distress. Her pulse as grossly irregular. Both lower extremities distal to the knees were very cold to the touch. The right foot was markedly cyanotic. Both feet exhibited as like pallor on elevation. No pulsation was palpable in either femoral, popliteal, posterior tibial, or dorsalis pedis arteries. The entire picture resembled that of block in the region of the bifurcation of the abdominal aorta. However the possibility of minor emboli with major degree of reflex vasospasm could not be readily ruled out, and, in view of her poor general condition, it was decided to employ conservative therapy. Within 7 hours, arterial pulsation had returned throughout the entire right lower extremity and within 2 weeks, excellent pulsation was palpable in the left femoral and popliteal arteries. At this time both feet were warm and of normal color. Symptoms had disappeared. Figure presents series of occlusometric tracings illustrating this remarkable degree of bilateral reflex vasospasm resulting from minor embolic occlusion of an artery in the distal portion of single extremity. Patient made an excellent recovery only to experience several months later (from cerebral emboli).

The vasospasm just described has important implications concerning treatment. As has been demonstrated, an embolus lodged in the distal portion of an extremity may reflexly render the more proximal and larger arteries pulseless. Unless the possibility of spasm is considered, these larger spastic vessels may be surgically explored for the purpose of removing what is erroneously considered to be the offending embolus.

A V., white female aged 26 years, came under observation April 8, 1940. She had suffered from rheumatic carditis with fibrillation for many years, but as well controlled. While convalescing from an elbow operation, she suddenly experienced an acute severe pain in her right leg and foot accompanied by sensations of coldness and numbness.

The right foot and lower leg were mottled, very cold to the touch, and exhibited as-like pallor on elevation. Excellent pulsation as palpable in the right femoral artery, no pulsation was palpable in the popliteal artery or its branches. Occlusometric readings at the level of the popliteal space were zero. A diagnosis of an embolic occlusion of the right popliteal artery was made. Under local anesthesia, the popliteal artery was exposed. It was markedly constricted, its diameter measuring only 1/4 of an inch. The constricted vessel exhibited extremely faint pulsation and contained no thrombus. No attempt was made to explore the artery. The wound was closed and conservative therapy as instituted. Within 24 hours, the foot as pink and warm and symptoms had subsided. She made an excellent anatomical and functional recovery and has remained well.

Another important bearing on treatment concerns the use of heat. It has been demonstrated (1, 2, 5) that external heat stimulates the metabolic activity of ischemic tissue and hastens the onset of gangrene. Therefore, when the collateral circulation in an extremity rendered acutely ischemic is so spastic it cannot relax in response to the huge concentration of vasodilating substances surrounding it, the use of heat as an additional dilating stimulus is, under the circumstances not only illogical but dangerous.

During the acute stage of an embolic occlusion, therapy should concern itself with relaxing spastic vessels and preventing their thrombosis. To secure the desired relaxation, intravenous injections of papaverine hydrochloride in $\frac{1}{2}$ grain doses every 4 hours for 48 hours and then 3 times a day for a week are almost specific (4). To prevent thrombosis of the collateral circulation pending its dilatation, and to prevent spreading thrombus formation starting at the site of the actual organic occlusion, heparin is administered (3, 6, 7, 8, 9, 10). Since many of these patients are cardiacs, heparin can rarely be administered in a continuous intravenous infusion of saline as is the usual procedure. Instead, it must be given intravenously in 4 hour doses of 50 milligrams each. This dosage may have to be adjusted to keep the blood clotting time at a minimum level of 15 minutes.

The limb is swathed in cotton and protected with an unlighted cradle. After spasm has disappeared, as indicated by an increase in the surface temperature of the foot, an improvement in its color, and subsidence of symptoms, measures may be instituted for the purpose of further stimulating the flow of blood through collateral channels. Mild local heat, the rhythmic venous occlusion machine, and the suction-pressure boot may now be safely employed.

Should the ischemia fail to improve or become progressively severe despite the administration of papaverine and heparin, an actual organic block of a major vessel must be considered and an embolectomy with the patient still heparinized performed.

Individuals who have sustained an embolic occlusion may present themselves for treatment several weeks after the acute vascular accident has occurred. In such instances, it is often found that a periarthritis involving the thrombosed vessel is stimulating afferent sympathetic neurones with resultant pain or reflex spasm of the collateral bed. Resection of the offending thrombosed arterial segment is indicated. The following cases are illustrative.

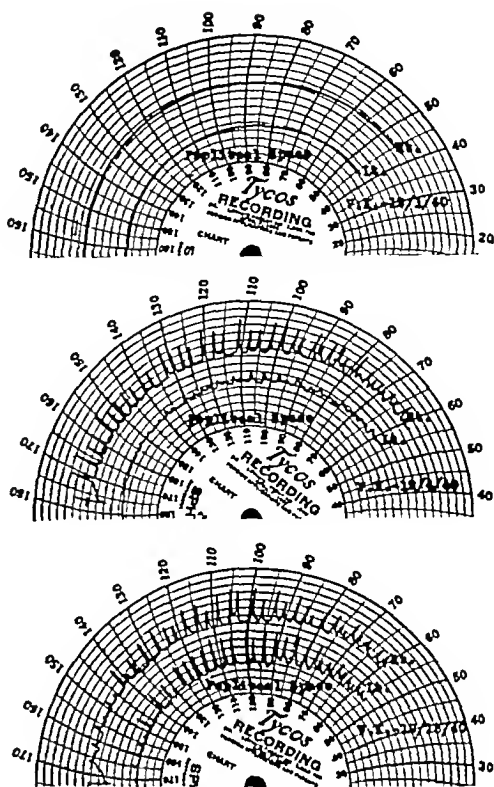


Fig 1. A series of tracings taken with a recording oscilometer depicting the remarkable degree of bilateral vasospasm which may result from an embolic occlusion of an artery in the distal portion of a single extremity. Tracing taken December 1, 1940, 1 hour following embolic occlusion of artery in distal portion of left leg, reveals absence of pulsation in each popliteal space. Tracing taken December 4, 1940, 72 hours following acute vascular accident, reveals excellent pulsation in right popliteal space and slight pulsation in left popliteal space. Tracing taken December 15, 1940, 2 weeks following occlusion, reveals excellent and equal pulsation in each popliteal space. Conservative treatment employed throughout. Note irregularity in magnitude and spacing of pulsation due to auricular fibrillation.

M. B., a white male aged 48 years, came under observation March 27, 1939. He had suffered from rheumatic heart disease for many years and was subject to bouts of fibrillation. About 10 days before I saw him, he experienced sudden severe pain in both feet accompanied by sensations of coldness and numbness. Since then, he had been incapacitated by a peculiar type of pain referred to the calves of his legs. The pain was present constantly and was worse at night. He described the pain as "squeezing" as if the calves of his legs were caught in a closing vise. The pain was so severe that morphine gave only transient relief. He also suffered from pain, coldness and numbness of the feet but to a lesser degree.

Both feet were cold to the touch, somewhat cyanotic, and exhibited pallor on elevation. There was no tissue necrosis. Excellent pulsation could be felt in each common femoral artery down to its bifurcation. No pulsation could be detected either manually or with the oscilometer distal



Fig. 1. Left. Low power magnification of microscopic section of segment of thrombosed superficial femoral artery and adherent femoral vein resected. Cells after acute embolic occlusion. Sections show striking changes in femoral artery and complete occlusion of lumen by thrombus mass composed in great part of red blood cells and fibrin. The intima in places is thickened and shows degenerative changes. The media likewise shows degenerative changes. The adventitia and regional tissues show moderate to considerable round cell infiltration and some edema. The veins in the section show some thickening of the walls and some round cell infiltration and edema of the outer coats and regional tissues. A small nerve in this section shows some edema and round cell infiltration especially perineural. Diagnosis: Femoral artery occluded by recent thrombus.



Fig. 2. Low power magnification of microscopic section of thrombosed brachial artery resected. Cells after acute embolic occlusion. Section shows the wall of the artery to be somewhat thickened. Most of the thickening is due to reaction in the serosa. The lumen is filled with blood that has undergone considerable stasis. Intermingled with the blood are fibrin strands. There is moderate amount of fibroblastic activity between the clot and the vessel wall. The adventitial coat is considerably thickened and there is noted fibroblastic activity. There is also present moderate amount of regional round cell infiltration. Diagnosis: Organizing embolus of brachial artery with acute periarthritis.

to these points. The calf muscles are relaxed and flabby. The symptoms in the feet are interpreted as being of ischemic origin. Like the calves suggested stimulation of intravascular and perivascular sympathetic nerve fibres. Accordingly under local infiltration anesthesia, the proximal portion of each superficial femoral artery is exposed for the purpose of performing an adventitial stripping. However this proved to be impossible because of inflammatory adhesions between the thrombosed arteries and the adjacent femoral veins. The arteries are opened and the thrombi found to be adherent. A small section of each thrombosed artery and adherent vein is excised (Fig. 1). The operation gives immediate and complete relief of the pain in the calf as of his leg. Subsequently measures are instituted to stimulate the growth of collateral circulation. He recovered complete use of his extremities and has been well since.

P. D., 41 years old, male, aged 41 years, came under observation February 2, 1941. About 2 weeks before admission he experienced sudden severe pain in the antecubital space of his right arm. The pain rapidly spread up the inner aspect of his right arm, and the hand became cold and numb and began to ache. The pain, coldness, and numbness in hand became increasingly severe, the end of the thumb and forefinger became black, and finally "necrosis" of the fingers was lost.

Medical consultation revealed the presence of an aortic valvulitis with questionable congenital heart disease. X-ray as negative for cervical ribs. The right hand, as for cold, empty, cyanotic, and assumed as like pulse on elevation. Cutaneous sensibility as absent, and the patient was unable to move his fingers. The distal phalanges of the first and second fingers are gangrenous. The radial and ulnar arteries are pulseless. Oscillometric readings at the level of the right forearm are zero. The entire length of the brachial artery from its junction with the axillary down to its bifurcation as palpable as pulseless tender cord like structure. It is felt that the thrombosed vessel undergoes rise to reflex spasm of the collateral circulation to the hand. Accordingly under general anesthesia, the entire length of the brachial artery is exposed. It is completely thrombosed. The artery is opened, and the thrombus was found to be adherent. Feeble pulsation is present in the terminal portion of the axillary artery. The thrombosed brachial artery is severed at its junction with the feebly pulsating axillary. Within minutes, the distal stump of the axillary artery dilated and began to pulsate vigorously. The entire length of the thrombosed brachial artery is excised (Fig. 2). Twenty-eight hours later the patient is able to move his fingers, sensibility had returned, the hand is pink and warm, and symptoms had

disappeared. About 3 weeks after operation, he suffered a right cerebral embolus with complete left hemiplegia. He survived this episode and is still living. The hemiplegia has remained. Fortunately, adequate function has been restored to the right hand, thus sparing the boy from total incapacitation.

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GASTROSTOMY—JEJUNAL INTUBATION

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GASTRIC surgery is still attended by primary mortality and morbidity which is not commensurate with the magnitude of the operations. Hospital mortality rates vary from 10 to 20 per cent as shown in recent reports from representative clinics. From the evidence which is constantly accumulating, it is becoming more and more apparent that much of this excessive mortality is the result of malnutrition which is present to a minor degree in all and to a severe degree in many of the patients subjected to gastric operations. Only recently has there developed an appreciation of the extent of this depletion of such vital nutritional elements as plasma proteins and vitamins and the far reaching influence of these deficiencies upon the repair of tissues, upon gastric and intestinal motility, and upon the distribution of fluids.

In autopsy reports many of the deaths are attributed to the pathological findings which are immediately apparent but which in reality are often secondary to nutritional deficiencies. For example, when a patient who has depleted his food stores by starvation resulting from pyloric obstruction dies following operation, the autopsy may reveal such obvious causes of death as pulmonary edema, or as peritonitis resulting from leakage from the line of suture. In all probability, however, the edema resulted from hypoproteinemia or the leakage from the failure of tissue repair caused by protein, vitamin C, and possibly other unknown deficiencies.

In most of these malnourished patients it is impossible to replenish their depleted food stores before operation is undertaken and one can at best provide only a very temporary supply of certain essential elements. To this end, however,

all available facilities for rehabilitation, such as the liberal administration of water, sugar, whole blood, blood plasma and vitamins, should be utilized. Since the nutritional demands are tremendously increased following operation and since the parenteral route meets these demands so inadequately, it is very important to provide nourishment as soon as possible by alimentation. This can be done starting immediately following operation by means of oral jejunal feedings. Following Ravdin's report approximately 3 years ago, the method with technical variations has been used by me almost routinely. In the earlier cases two Levine tubes were threaded into the stomach, one through each nostril before the operation was started. At the completion of the gastrojejunal anastomosis one of these tubes was threaded through the stoma into the distal loop of the jejunum for a distance of 8 to 12 inches. Through this tube feedings were administered every hour, starting as soon as the patient returned from the operating room. Each feeding consists of 2 to 4 ounces of peptonized skimmed milk containing 5 grams of glucose to each 100 cubic centimeters of the mixture, followed in some instances by 1 or 2 ounces of normal salt solution, as indicated, to maintain fluid balance. By this means alone the patient receives from 2800 cubic centimeters of fluids to as large quantities as desired in addition to the normal salt requirements, so that it is unnecessary to administer fluids parenterally. In addition these feedings provide in 24 hours 150 grams of glucose, an equal quantity of milk sugar, 95 grams of the much needed protein, and the minimal caloric requirement of 1,795 calories. To these feedings there has been added the vitamins B-complex and C in the quantities indicated, and other medications as desired. Because 2 patients pulled



Fig. Oral jejunal intubation for feeding. Three days after an anterior Polya resection showing the two Levine tubes which were threaded into the stomach (one through each nostril) before operation. At operation one tube was threaded through the stomach, *S*, into the distal loop of the jejunum, the other one was left in the gastric stump in order to keep it empty by constant suction. The area of increased density between *O* and *S* represents the thick edematous walls of the stomach and jejunum around the stoma.



Fig. Gastrostomy jejunal intubation for feeding. Roentgenogram taken 7 days after gastroenterostomy to relieve pyloric obstruction due to postcholecystectomy distention about the duodenum. The tube enters the abdomen at *A*, the stomach at *B*, and the jejunum through the stoma at *S*. Note the area of decreased density outlining the enormously dilated stomach. A small amount of barium taken by mouth outlines the cardia. In some barium is jetted through jejunal tube can be seen in jejunum. Incidentally shadow of its right renal calculus is shown.

out the Levine tubes unintentionally during sleep the original procedure has been modified in the malnourished patients as shown in the roentgenogram, Figure

After the gastrojejunal anastomosis is completed a catheter gastrostomy is done and the tip of a catheter is threaded through the stoma into the distal segment of the jejunum. The wall of the stomach at the site of gastrostomy is anchored to the abdominal wall and the proximal end of the catheter is brought out through stab wound to the left of the incision. It has been learned that the catheter can be passed most simply through the stoma into the jejunum by grasping the tip of the catheter in a curved hemostat with which it is directed through the small gastrostomy incision into the jejunum. Through this catheter feedings are administered as has previously been described.

If the jejunum is distended rapidly some discomfort may be produced. Therefore the feedings are administered slowly drop by drop from a

gravity bottle. The stomach is kept empty by constant suction applied through the Levine tube in the stomach.

Two ounces of water are given by mouth every hour. This serves two purposes. It pleases the patient and, as it returns through the Levine tube, it washes the stomach and the tube. On the third day suction is discontinued, but the tube is left in place so that suction can be resumed in case of distress or other evidence that the stomach has failed to empty. On the fourth day hourly feedings of ounces of milk and cream in addition to water are given by mouth and the jejunal feedings are reduced to 2 ounces. On the 5th day a 6 meal bland gastric diet is started and jejunal feedings are discontinued. If oral feeding progresses satisfactorily the gastrostomy catheter is removed on the 7th or 8th day.

This method of intubating the jejunum has certain advantages over jejunostomy. It does not fix the jejunum to the abdominal wall or cause other adhesions about it to act as potential sources of

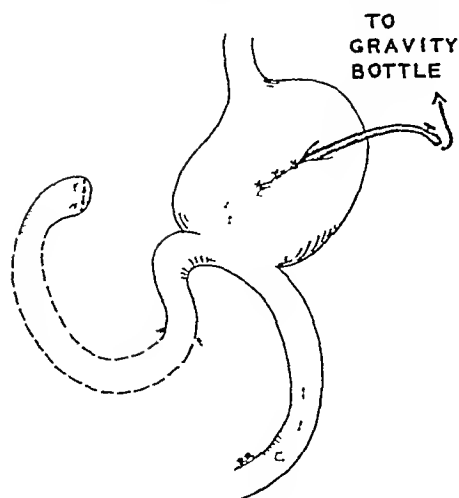


Fig 3 Gastrostomy jejunal intubation supplementing gastric resection.

jejunal obstruction and there is less likelihood of leakage

In our small series of cases no complications or ill effects have been encountered. To the contrary, convalescence in each case has been extraordinarily uneventful.

It is obvious that in cases with small residual gastric pouches which retract up under the costal margin, the procedure is technically impossible. In these cases recourse is had to oral jejunal feedings through the Levine tube which had been passed into the stomach before operation. Fortunately, however, little difficulty has been encountered in the severely malnourished patients who are most in need of immediate feeding because they are thin and lax from much loss of

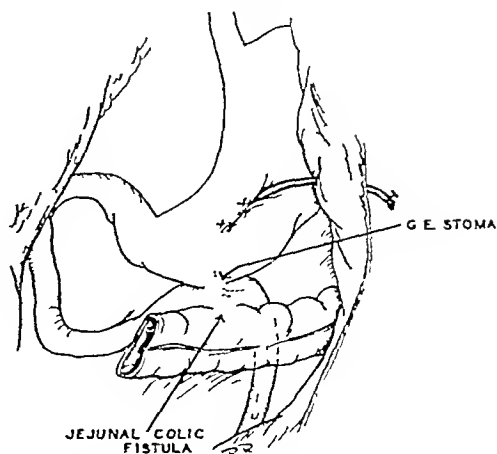


Fig 4 Gastrostomy-jejunal intubation for preliminary jejunal feeding of patients with gastrojejuno-colic fistula. The tube by-passes the jejunal-colic fistula and delivers food and water where it will be assimilated. After adequate restoration of nutrition the radical corrective operation can be done with much less risk.

weight and their stomachs are usually large as a result of obstruction.

Recently, jejunal feedings by means of gastrostomy-jejunal intubation have been used to rehabilitate a severely depleted patient with a gastrojejuno-colic fistula. A diagram of the procedure is shown in Figure 2. The rapidity of both physical and biochemical restoration was impressive as was the convalescence from the corrective operation which was done 12 days later. Following this corrective operation which included partial resection of the stomach, the gastrostomy tube was threaded into the jejunum through the new stoma and the jejunal feedings were continued.

MULTIPLE MYELOMA

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IN a previous communication two of us (Ghormley and Pollock) reviewed the clinical and laboratory findings in 86 cases of multiple myeloma encountered at the Mayo Clinic between January 1, 1924, and December 31, 1936. This present study was undertaken in an endeavor to bring the statistical survey of this disease up to date. Forty-one additional patients who had multiple myeloma were examined in the last 3 years, making a total of 127 patients examined and treated in the 16 years from January 1, 1924, to December 31, 1939. It is of interest to note the increase in the number of cases in which a diagnosis of multiple myeloma has been made since our paper on this subject was published.

Multiple myeloma is a highly malignant tumor of the bone marrow which tends to occur after the fifth decade of life. Although the disease generally is insidious in its onset, on occasion it may run a fulminating course. In one of our cases only 4 months elapsed from the appearance of the first symptom until the death of the patient.

The etiology is unknown. Men are affected about twice as frequently as women. Trauma does not appear to influence the onset of the disease although in several cases history of injury was elicited on inquiry. Its importance as an etiological factor was not emphasized by the patients. The original description made by Dalrymple in 1846 of the pathological findings cannot be improved. Speaking of the appearance of two vertebrae and a rib at necropsy he said "the disease appears to have commenced in the cancellated structure of the bone for the external osseous laminae are firmer and more healthy than the internal. . . and again, "the smoother surface of the rib however is rubbed by internal growths elevating the outer laminae here and there into irregularly sized and rounded dark red projections visible through the periosteal covering. The outer layers are steel hard requiring the exertion of some force to cut them; they are thin, however and, when sliced, expose large cancellous cavities filled by a red gelatiniform substance threaded here and there by fine bony fibers. It is in these fibers of still-existing bone that many of the more important morbid changes may be witnessed.

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Microscopically the tumors are made up predominantly of cells which closely resemble plasma cells. They possess the same tinctorial characteristics, which can be brought out by the Unna-Pappenheim stain. However the nuclei in these cells are more prominent than those in normal plasma cells. If a tumor nodule is the source of the material examined the histological appearance is uniform and comprised almost entirely of these cells. The myeloid tissue and fat spaces seen in normal marrow are not encountered. On the other hand, if a portion of marrow between tumor nodules is examined, the picture may be essentially normal except for the finding of isolated tumor cells or small nests of tumor cells.

Imprint preparations made from bone marrow obtained at biopsy or smears made from aspirated material, stained with any one of the Romanowsky combinations of stains, lend a somewhat different appearance to these cells. They vary in size from 7 to 30 microns and have a definite outline. They are usually oval but occasionally are somewhat irregular. The cytoplasm ordinarily is deeply basophilic and has a lighter staining zone adjacent to the nucleus. The nucleus is round or oval and has a variable type of nuclear structure, the chief characteristic of which is a large, conspicuous, sharply demarcated nucleolus. The chromatin usually is arranged either in fine or coarse strands, rarely in dense masses, and is sharply differentiated from the parachromatin. The identity of tumor cells in myeloma has not been established. Inasmuch as they differ from normal plasma cells and have a characteristic appearance morphologically, they are now usually referred to as "myeloma cells."

The progenitor of the myeloma cell is unknown. Many theories have been advanced and the cells which have been suggested as possible sources of these elements are as follows: myeloblasts, dysplastic hemocytoblasts, the reticuloendothelial cells, lymphocytes, megakaryoblasts and osteoblasts. From evidence in recent literature and in our material, it seems likely that in most instances the myeloma cell is derived from reticuloendothelium.

SYMPTOMS

The symptoms are diverse and, frequently apparently unrelated. There are no symptoms

which are pathognomonic of the disease. Of our entire series of 127 cases, only 32 were proved at pathological examination. Eighty-three of the patients were males and 44 were females. The oldest male was 75 years of age, the youngest 4 years. The average age of the patients at onset of symptoms was 54 years. The duration of symptoms at the time of the first examination at the clinic ranged from 3 weeks to 5 years. The average duration of symptoms was 1 year. The longest duration of the disease was 9 years, the shortest 4 months. Pathological fractures were present in 13 proved cases, 40.6 per cent.

Backache, by far the most common symptom, was the major complaint in most of our cases. When this was the sole symptom, the reason for the erroneous diagnosis of arthritis of the spinal column or neuritis is understood. Loss of strength and progressive weakness were the second most common cause for the patient's seeking advice. Anemia, loss of weight, or occurrence of a pathological fracture was described less frequently, and the presence of a palpable tumor was rare.

In about 70 per cent of our cases, albuminuria was present, although in only 36.5 per cent of cases in our second series was renal damage present, as evidenced by casts, hematuria, and an elevated value for blood urea. It is possible for a condition which has been diagnosed and treated as nephritis ultimately to be proved multiple myeloma. In one of our cases, excessive albuminuria of long standing was the only finding, on further investigation, Bence-Jones proteinuria was discovered. Results of sternal puncture, advised because of this finding, revealed the true nature of the disease as multiple myeloma. Investigation for Bence-Jones bodies was made in 112 of the 127 cases, with positive findings in 68, 60.7 per cent. A similar research in the proved group of cases of multiple myeloma gave positive findings in only 12 of the 29, 41.3 per cent. The more important of the various investigations carried out are listed in Table I.

DIAGNOSIS

Although symptoms are not pathognomonic of this disease, the discovery at examination of several of the findings listed in Table I should suggest the possible diagnosis of multiple myeloma.

Biopsy or sternal aspiration to confirm the diagnosis of multiple myeloma is warranted in cases in which the patient is a man more than 50 years of age who has changes in bones and progressively severe backache associated with Bence-Jones proteinuria or high level of protein in the serum. Multiple, punched-out areas of de-

TABLE I — SUMMARY OF DATA CONCERNING CONSTITUENTS OF BLOOD IN ENTIRE SERIES

Investigation	Estimations*	Abnormal results		
		Type	Cases	Per cent
Albumin-globulin ratio	23	Reversed	13	56.5
Uric acid	6	Elevated	4	66.6
Blood cholesterol	5	Reduced	3	60
Blood calcium	48	Elevated	10	20.8
Blood phosphorus	42	Elevated	4	9.5
Blood phosphatase	22	Elevated	4	18.1
Serum sulfate	16	Elevated	5	31.2
Serum protein	20	Elevated	10	50
Blood urea	57	Elevated	21	36.8
Sedimentation rate	29	Elevated	23	79.3
Blood creatinine	9	Elevated	5	55.5
Bence-Jones protein in urine	112	Positive	68	60.7

*One estimation listed per case

struction in the skull, ribs, and spinal column usually are accepted as roentgenological evidence of multiple myeloma, but it must be recognized that widespread metastatic carcinoma may give rise to similar appearances. In this connection, it is well to remember that the presence of myeloid immaturity and a "greasy" appearance in the blood smears described as suggestive of multiple myeloma are found in metastatic malignant disease which involves the bone marrow and also in paroxysmal hemoglobinuria. Magnus-Levy admitted the possibility of Bence-Jones proteinuria resulting from activity of normal marrow.

The condition of the patient is not always an index of the extent of the disease. We have been astonished to observe patients in comparatively good condition who had extensive skeletal destruction and again, we have been embarrassed at our inability to discover a definite skeletal focus on examination of a patient who is dying and has all other clinical signs and evidences of multiple myeloma. With so many possibilities for error, accurate diagnosis is difficult. The diagnostic results of biopsy are excellent, but many patients are reluctant to undergo a surgical procedure which is not calculated to give relief.

The comparatively recent introduction of sternal aspiration has placed at our disposal a procedure which will permit accurate diagnosis in most cases. The method is so simple in application that its routine use in suspected cases should be possible. Material is aspirated from the marrow cavity of the sternum by means of a dry syringe

and is placed in a 2 cubic centimeter paraffin lined test tube containing a small amount of heparin. Material is mixed well to prevent clotting. Smears are made from this material which are stained with Wright's stain and then by Giemsa's. The presence of myeloma cells is diagnostic of the condition but their absence does not rule it out.

PROGNOSIS

Prognosis is uniformly poor in all cases in which evidence of involvement of bone is present. In our entire series, the average duration of life after diagnosis had been made was a year which conforms fairly accurately to the figure of 14.05 months which we gave originally in our proved series. The longest duration of the disease in our proved group of cases was 9 years and 2 months, and the shortest, 4 months.

In cases in which multiple myeloma affects the soft tissues only it is possible that complete extirpation of the lesion will result in cure.

Other therapeutic measures are foredoomed to failure, yet there is evidence from the follow up reports of our patients that temporary relief and improvement have followed the use of roentgen therapy and general tonic measures. At this time the authors are unable to state whether the patients' lives have been prolonged materially by the use of these measures.

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THE SURGICAL ANATOMY OF THE SUPERIOR HYPOGASTRIC PLEXUS

With a Report of 150 Personal Dissections

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SINCE its existence was first noted by von Haller many anatomists and surgeons have studied and given varied names and descriptions to that collection of sympathetic fibers which only of late is being designated properly as the "superior hypogastric plexus." This plexus, which is rarely a single nerve and is always prelumbar, is commonly and erroneously referred to by the misleading term, "the presacral nerve" (Latarjet and Bonnet). Recently Davis (23-26), Labate (38) and others have stressed the inaccuracy of the term "presacral" and have come to popularize the more acceptable terminology of Sappey, "superior hypogastric plexus."

In 1925 Cotte introduced the operation of resection of the superior hypogastric plexus for the relief of pelvic neuralgia, vaginismus, dysmenorrhea, hypoplasia of the uterus, metrorrhagia and sexual neurosis (2-3). Subsequently the procedure was popularized and the indications for its use extended by numerous contributions, particularly those of Cotte (5-20) and of Leriche (44-46). The successful and widespread use of extirpation of the superior hypogastric plexus led to its adoption for the relief of pain arising from such varied pathological conditions as (a) inoperable carcinoma of the pelvic viscera, (b) intractable primary dysmenorrhea, (c) cord bladder, (d) intractable cystalgia, (e) spasm of the bladder neck, (f) obstruction of rectal origin, (g) Hirschsprung's disease, (h) pruritus vulvae, (i) vaginismus, (j) dyspareunia, (k) sclerocystic degeneration of the ovaries, (l) kraurosis vulvae, (m) severe persistent postoperative pelvic pain, and pelvic and abdominal pain of obscure origin.

The increase in indications for extirpation of the superior hypogastric plexus and the wide adoption of the procedure as reflected by the numerous reports in recent literature created the need for, and gave a marked stimulus to, the study of the available literature on the detailed anatomy and surgical anatomy of the plexus. This was found to contain many conflicting reports. In fact, after

noting the repetition of inaccuracies contained in the older literature one is tempted to agree with Byron Robinson when he states "It would astonish any student to know how little has been published in regard to the nervous system of the female genitals that is of an original character."

The existence, in the literature, of this wide variety of descriptions of the plexus led to a series of careful studies by a number of recent investigators, but as Davis (23-26) has so well stated, "Painstaking and exhaustive though this work has been, and possibly because of these factors the variations in the findings of different writers on the morphology of the plexus are even wider than those exhibited by the older authors."

While all types of plexus patterns have been reported, the main conflict lies between those who have reported the predominance or sole existence of "presacral nerves" and those who have substantiated the finding of a predominance of "superior hypogastric plexuses." An understanding of the development of these differences can be derived from an appreciation of the fact that single nerves, bilateral cords, and a multiple variety of plexus formations occur, and when an investigator has had occasion to report a short series of dissections in which a single type predominates there is apt to be an emphasis on that type, whereas the result of a larger series would at once demonstrate that all varieties reported may occur, and that the plexus patterns predominate. It is also true that superficial and inadequate dissection will frequently reveal a single nerve or bilateral cord, whereas further careful dissection of the same subject will reveal many intercommunicating twigs and may uncover a typical plexus arrangement. It is hoped that this investigation, containing as it does the largest group of detailed dissections thus far reported, will tend to crystallize more clearly our concept of the morphology of the superior hypogastric plexus.

MATERIAL AND METHODS OF STUDY

The specimens included in this study were obtained from the routine cadaveric material in the department of gross anatomy, Tulane Univer-

From the Departments of Gross Anatomy and Gynecology
Tulane University, School of Medicine.

sity during the summer sessions 1938 and 1939 and the regular sessions 1938-1939 and 1939-1940, which were made available by Dr. Wilbur C. Smith and also several autopsy specimens from Toussaint Infirmary, New Orleans, were provided through the courtesy of Dr. John A. Lanford. While 10 dissections were done on infants in order to determine whether there are differences in the morphology of the plexus in the infant and the adult, as claimed by some investigators, none was found and the infant material is not included in this report. This report considers the findings in 150 adult dissections, representing 90 females and 130 males. Of the 90 females 14 were negro and 6 white, while 96 of the male specimens were negro and 34 white. This preponderance of the negro material is in accord with the usual percentage distribution in the anatomical material obtained by this laboratory and though there are many interesting studies on anatomical and surgical peculiarities in the negro, particularly those of Matas, Souchon and Hoffman, there appeared to be no differences in the morphology of the superior hypogastric plexus in the two races and therefore for statistical purposes the group will be considered as a whole throughout the following discussion.

Detailed dissections of the entire abdominal and pelvic sympathetic system were made on the first 33 cadavers. This included a study of the celiac plexus, the aortic plexus, the ovarian and renal plexuses, the lumbar sympathetic trunks, and the superior hypogastric plexus. The connections of the superior hypogastric plexus, including all of its afferent and efferent fibers, with the ganglionated sympathetic trunk and the sympathetic ganglia proper were studied. The fibers were traced from their origins to their final distribution in the pelvic viscera. In the remaining subjects the detailed gross anatomy of the superior hypogastric plexus and the interiliac trigone was recorded with notations on the occurrence of anomalous structures in the interiliac trigone. In every instance a record was made of the size of the interiliac trigone and a sketch made of the morphology of the plexus and the relationships existing between the plexus and the contents of the interiliac trigone. In addition, observations were made on the variations of the sigmoid mesocolon. The female subjects, in every instance, were submitted to detailed study.

CONNECTIONS OF THE SUPERIOR HYPOGASTRIC PLEXUS

The superior hypogastric plexus is a direct downward continuation of the intermesenteric

nerves of Petit Dutaillis-Glandin. By way of these nerves it is connected above with the celiac plexus and the lumbar sympathetic ganglia (upper or 3). The intermesenteric nerves are composed of several (2 to 6) parallel fibers on either side of the aorta. These parallel fibers are connected by innumerable fibers and form the later mesenteric or aortic plexus. The intermesenteric nerves arise from the renal or aorticorenal ganglion, the periaortic plexus of the renal artery and the transverse aortic bar and the first and second lumbar sympathetic ganglia. They at first lie on the lateral aspect of the aorta, the right being somewhat further lateral than the left, which is closely adherent to the lateral aspect of the aorta. They then pass downward and medially to the anterior surface of the aorta, on which they continue downward (receiving and distributing fibers to the inferior mesenteric ganglion and plexus) to the bifurcation of the abdominal aorta at which level they enter the interiliac trigone and terminate by forming the superior hypogastric plexus. Just prior to their termination they receive fibers from the lower lumbar ganglia.

The plexus is connected above with the inferior mesenteric periaortic plexus, and when present the inferior mesenteric ganglion. These fibers may run downward to join the plexus directly or may join the intermesenteric nerves.

The superior hypogastric plexus receives fine branches from each of the lumbar sympathetic ganglia. The contribution of the superior (first and second) ganglia is usually the more marked, frequently consisting of several distinct fibers which are contributed to the plexus via the later mesenteric nerves. The fibers from the inferior ganglia are inconstant and of finer caliber and when present are of a lesser number than the superior. The branches from the inferior lumbar ganglia occasionally join the intermesenteric nerves but more frequently enter directly into the superior hypogastric plexus, being found inferior to the termination of the intermesenteric nerves in the superior hypogastric plexus. The number of ganglia in the lumbar section of the cord varies, hence the terms superior and inferior ganglia are used in preference to numerical designations. However in every case fibers are contributed to the plexus by all the lumbar sympathetic ganglia. The preponderance of fibers from the upper lumbar ganglia is in keeping with the observations of Hovelacque, Delmas and Lenoir, Davis, Labatte, and others.

In addition to these twigs from the lumbar sympathetic ganglia, fine fibers running from the sympathetic trunk proper to the superior hypo-

gastric plexus were demonstrable in 3 instances. The rarity of these fibers is in keeping with the finding of Davis, and contrasts with their frequency as reported by Latarjet and Bonnet. Of the 3 dissections in which these were seen, they occurred bilaterally in 2 instances and only on the left in 1 instance. All were short, fine fibers and ran almost transversely from sympathetic trunk to superior hypogastric plexus.

The fibers arising from the lumbar sympathetic ganglia proper emerge from the medial aspect of the ganglia as fine though extremely tough filaments which are usually single, though occasionally multiple. They course downward and medially posterior to the common iliac artery of that side and anterior to the vein. This relationship of artery, nerve, and vein is quite constant though in 5 dissections the nerve fibers passed posterior to both the artery and vein, and in 3 instances the fibers passed anterior to both structures. The nerves enter posteriorly at the superior aspect of the superior hypogastric plexus. In specimens in which a single "presacral nerve" occurs the fibers usually join the lateral borders of the nerve cord. In instances in which bilateral nerve cords occur, fibers join the lateral aspect of the ipsilateral nerve cord, while in the usual instance these nerves join the lateralmost portions of the plexus.

The sacral ganglia do not usually contribute fibers to the superior hypogastric plexus, though in some instances the first sacral ganglia may supply the plexus (6 per cent). Where this occurred the fibers arising from the first sacral ganglion coursed obliquely upward from the ganglion to join the plexus. In 2 instances short horizontal fibers from the first sacral ganglion joined the superior hypogastric plexus in addition to a full complement from the lumbar ganglion. The sacral ganglia usually intercommunicate via short, fine filaments which are immediately prevertebral and posterior to the fibroadipose lamina containing the fibers of the superior hypogastric plexus (41). The sacral nerves contribute many fibers to the lateral aspect of the Frankenhauser plexus.

The larger portion of the fibers of the plexus gradually diverge toward the lateral aspect of the interiliac trigone to terminate in the paired inferior hypogastric nerves. The chief innervation of the ureter is derived from these nerves. The inferior hypogastric nerves continue antero-inferiorly on the lateral pelvic wall and enter the uterosacral ligaments through which they course to the lateral aspect of the rectal ampulla, to terminate in the plexus of Frankenhauser. This rich sympathetic nerve fiber content of the uterosacral ligaments has not been sufficiently appreci-

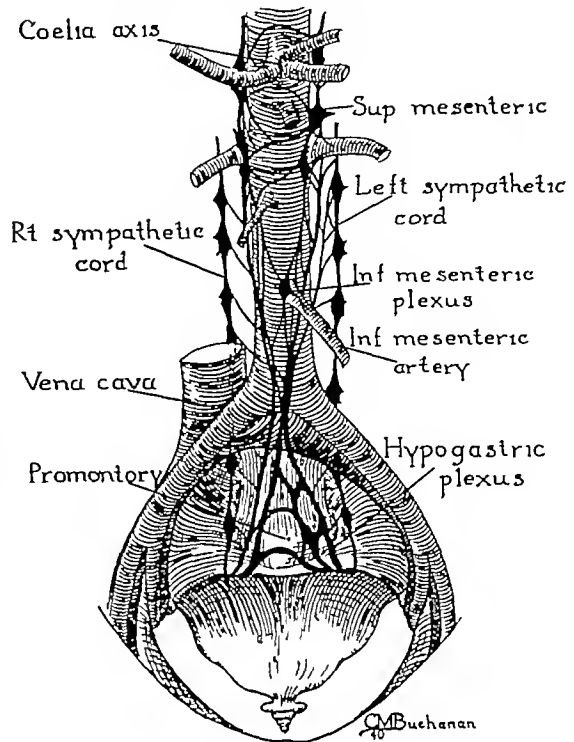


Fig 1

ated and is of considerable clinical interest since one frequently observes edematous and especially tender uterosacral ligaments associated with various types of pelvic pathology.

There has been considerable discussion in the literature as to the existence of the Lee-Frankenhauser ganglion or plexus. Hovelacque referred to the anterior portion of the inferior hypogastric plexus as "the so called ganglion of Frankenhauser." Lee, Frankenhauser, Robinson, Hashimoto, Jung, and Kehrer have all described the mass as a true sympathetic ganglion. It has been described as a grayish white plexus in the form of a quadrilateral mass whose limits and dimensions are not fixed, the medial surface of which is joined by the inferior hypogastric nerve. From the mesial aspect the pelvic visceral sympathetic innervation is derived, while the lateral aspect has an extensive anastomosis with the sacral nerves. Beautiful illustrations of dissections of the Frankenhauser plexus are given by Fontaine and Herrmann. The existence of this plexus, now well demonstrated anatomically, has been confirmed clinically by successful novocain and alcoholic block of the Frankenhauser plexus area which is an accepted surgical procedure.

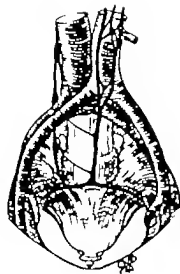


Fig. 2.

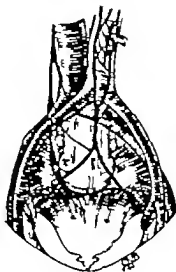


Fig. 3.

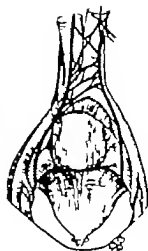


Fig. 4.

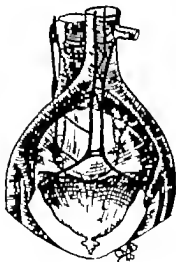


Fig. 5.

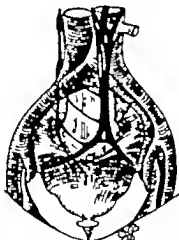


Fig. 6.



Fig. 7.

The superior hypogastric plexus also contributes filaments to the periarterial plexuses of the neighboring arteries: superior hemorrhoidal, the middle sacral, the external iliac and all the branches of the hypogastric.

The several fine filaments to the superior hemorrhoidal artery pass laterally from the superior portion of the left aspect of the superior hypogastric plexus and enter the sigmoid mesocolon. They are distributed to the sigmoid and may send fine branches to the plexus of Frankenhauser.

Infrequently fine filaments join the middle sacral periarterial plexus. This is occasionally true of fibers to the external iliac artery (demonstrable in only 7 instances). The rarity of this occurrence coincides with the report of Davis who takes issue with the report of Latarjet and Bonnet in which these fibers were discussed as though a common finding.

A diagrammatic schema of the connections of the superior hypogastric plexus is given in Figure

The sensory or afferent fibers course in a manner which probably is similar to that of the

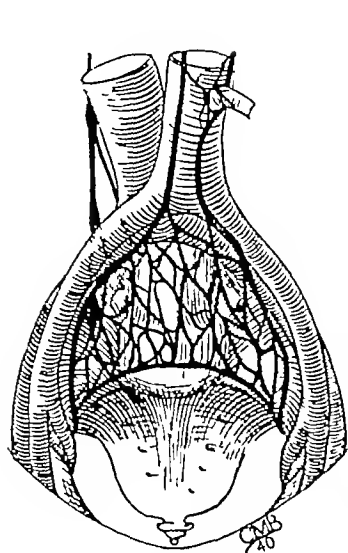


Fig 8

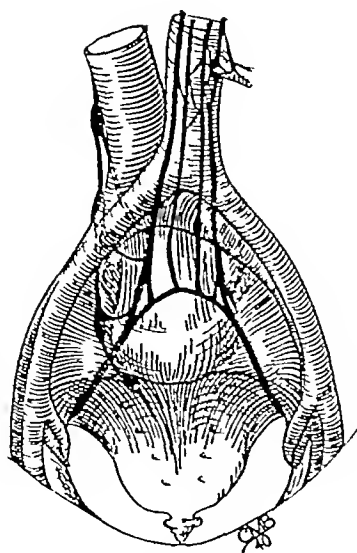


Fig 9

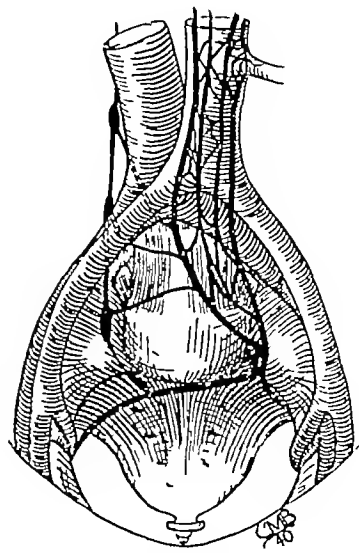


Fig 10

motor, or efferents, except that they go via the posterior roots to reach the nerve cells of the posterior root ganglia. The afferent fibers of all the pelvic viscera transverse the superior hypogastric plexus with the exception of the ovarian and possibly some of the fibers of the fallopian tube which according to the physiological and anatomical researches of Labate and Reynolds "have no connection by way of the superior hypogastric plexus, nor do they traverse the inferior mesenteric ganglia or the lower aortic plexus" (38). This observation is of considerable clinical importance, and is borne out by the results of sympathetic nerve block. The wider recognition of this contribution will call a halt to the needless (and of course unsuccessful) attempts to relieve pain of ovarian origin by superior hypogastric sympathectomy. The afferent nerves from the ovary are contained in the periarterial ovarian plexus and reach the tenth thoracic level of the spinal cord (Kuntz). The ovarian plexus is found in the suspensory ligament of the ovary and is joined by an external tubular branch from the fallopian tube. Five or six efferents of the tubular branch course through the broad ligament and reach the lateral aspect of the periarterial uterine plexus.

The uterine afferent fibers traverse the Frankenhauser and then the superior hypogastric plexuses to reach the cord at the level of the first lumbar to tenth thoracic segment (Kuntz). A detailed and excellent résumé of our current knowledge of the innervation of the uterus is given by Reynolds while a clear exposition of the inner-

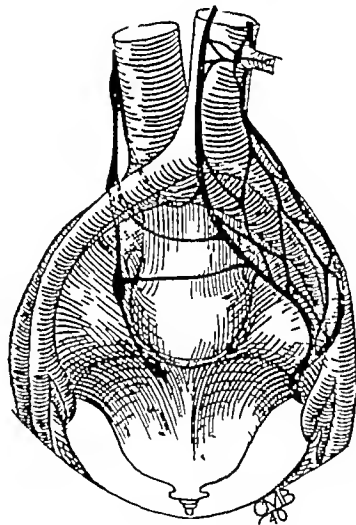


Fig 11

vation of the bladder may be found in McLellan's excellent monograph.

MORPHOLOGY OF THE PLEXUS

The superior hypogastric plexus is always found within the interiliac trigone, an area bounded by the bifurcation of the aorta above, the common iliac arteries laterally, and a line connecting these vessels at the promontory of the sacrum below. There is usually a plexus, uncommonly bilateral cords, and rarely a single "presacral" nerve. The plexus is triangular in shape with its apex up-

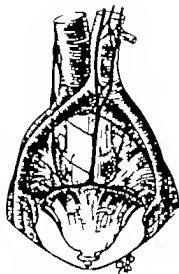


Fig. 2.

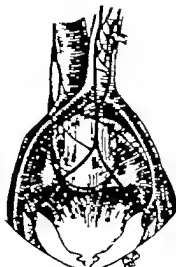


Fig. 3.

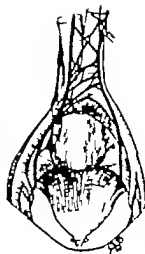


Fig. 4.

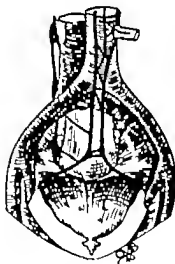


Fig. 5

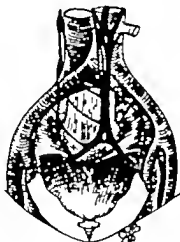


Fig. 6.



Fig. 7

The superior hypogastric plexus also contributes filaments to the periaortic plexuses of the neighboring arteries superior hemorrhoidal, the middle sacral, the external iliac and all the branches of the hypogastric.

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A diagrammatic schema of the connections of the superior hypogastric plexus is given in Figure 1.

The sensory or afferent, fibers course in a manner which probably is similar to that of the

mately 0.3 cm) The width of the base of the trigone averages approximately 7 centimeters (5.8 to 7.5 cm) and tends to be wider in the female than in the male (by approximately 0.5 cm) This is in keeping with the normal divergence of the common iliac arteries from the bifurcation of the abdominal aorta, which occurs at an angle of 60 degrees in the male and 68 degrees in the female It is of interest to note that the dimensions of the trigone were exactly similar in the negro and white female, however, in males the trigone tends to be narrower and longer in the negro than in the white

The trigone normally contains the left common iliac vein, the middle sacral artery and veins, and the right ureter On the left border of the trigone the inferior mesenteric artery and its sigmoid branch enter the root of the pelvic mesocolon Finally, a fairly tough retroperitoneal connective tissue layer, into which the fibers of the superior hypogastric plexus are incorporated, lies within this area

The left common iliac vein runs parallel to the inferior (medial) margin of the left common iliac artery and courses upward and to the right, ascending posterior to the right common iliac artery to join the right common iliac vein in the formation of the vena cava The left common iliac vein thus occupies a considerable portion of the upper and left aspect of the trigone The vein is immediately subjacent to the overlying (anterior) layer of fibrous and fatty tissue in which the fibers of the superior hypogastric plexus are found and thus constitutes a surgical hazard of marked importance, especially when it is remembered that the wall of the vein is extremely thin Fortunately, the fibrocellular layer which is firmly adherent in the remainder of the trigone is very loosely adherent to the vein and may be easily separated from it. An appreciation of the surgical importance of this fact is heightened when it is recalled that in 9 per cent of this series the entire superior hypogastric plexus is shifted to the left and occupies an area solely in the left half of the trigone being markedly condensed anterior to the left common iliac vein In performing a superior hypogastric sympathectomy the surgeon working "over" (i.e., anterior to) the vein takes advantage of this loose connection of the nerves to the vein, in an effort to avoid injury to the vessel Injury to the vein has been reported (1)

The middle sacral artery and its accompanying veins descend from the bifurcation of the aorta to the tip of the coccyx The artery passes downward in the interiliac trigone which it tends to bisect, though occasionally it occupies a position

slightly in the left half of the trigone Within the trigone it lies successively upon the intervertebral disc between the fourth and fifth lumbar vertebrae, and the anterior aspect of the body of the fifth lumbar vertebra It is posterior to the connective tissue layer which contains the nerve fibers, and may be palpated through this layer The artery is not infrequently confused with a "single presacral nerve" type of superior hypogastric plexus and occasionally has been extirpated for the plexus It is interesting to note that the artery which is *not frequently visually obvious* can almost invariably be palpated, while the *nerve fibers* of the superior hypogastric plexus which *are frequently visually obvious* through a transparent peritoneum can not be identified by the palpating finger When this point is appreciated more fully, the incidence of extirpation of the middle sacral artery for the "presacral nerve" will markedly decrease An appreciation of the fact that the existence of a "presacral nerve" is in itself a rarity will also cause a cessation of the extirpation of a single cord area, and lead to the universal adoption of the policy of extirpating the entire interiliac fibrocellular tissue for removal of the superior hypogastric sympathetic plexus

The right ureter is exposed in the interiliac trigone, where it crosses the right common iliac artery just superior to its bifurcation into the external iliac and hypogastric arteries Fortunately, the right ureter is firmly adherent to the posterior surface of the peritoneum and is usually retracted with the peritoneum when it is reflected laterally, whereas the nerve fibers are incorporated into and firmly adherent to the subjacent fibrocellular layer of retroperitoneal connective tissue Thus the ureter can be identified and injury to it avoided In certain instances in which a type III mesocolon exists (*vide infra*) and it is necessary to retract the mesocolon sharply to the left, or when a type II pelvic mesocolon exists which must be retracted far to the left in order to remove it from the operative field, the ureter may be displaced mesially and be more liable to injury The left ureter is normally found entirely outside of the interiliac trigone and is rarely subject to injury in superior hypogastric sympathectomy

The inferior mesenteric artery runs downward from its origin about 3.5 centimeters superior to the bifurcation of the aorta, running obliquely and to the left, anterior to the lower portion of the abdominal aorta, and the left common iliac artery It descends into the pelvis between the layers of the sigmoid mesocolon to terminate on the rectum as the superior hemorrhoidal artery Its sigmoid branches run downward and to the left to enter

ward, representing the convergence of the intermesenteric nerves, and its base inferiorly where the main groups of nerve fibers diverge to terminate in the inferior hypogastric nerves. The position of the nerves whether as single cords or various plexus patterns is always prelumbar and never presacral.

When the intermesenteric nerves fuse at the apex of the interiliac trigone and continue without divergence until the very base of the trigone the resultant pattern is a single nerve cord, the so called presacral nerve. This is relatively uncommon—3 per cent in this series (Fig. 2). Even this single presacral nerve pattern may be classified as a plexus, if one considers the microscopic studies of Elaut, who was able to demonstrate clearly in transverse sections of the interiliac fibroadipose layer at least 4 or 5 separate islets of nerve tissue which are lost in the fat infiltrated subperitoneal membrane and have no reciprocal connections. In 2 per cent of our dissections the intermesenteric nerves enter the trigone, slightly separated and after continuing down for 1 to 1.5 centimeters join to form a single nerve which bifurcates at the base of the trigone (Fig. 3). The intermesenteric nerves may enter the interiliac trigone widely separated and continue downward in this relationship to the base of the trigone where they continue as the inferior hypogastric nerves, thus giving a bilateral (or double) cord pattern (Fig. 4). When this occurs, the cords have a number of very fine filamentous connections demonstrable throughout the length of the interiliac trigone (8 per cent).

Plexus patterns occur (4 per cent) wherein the lateral components are sharply marked but there are numerous heavy connecting fibers, and though the nerve fibers when inadequately dissected appear as a single flat band, careful dissection reveals a plexus (Figs. 5 and 6).

In many instances (39 per cent) the intermesenteric nerves upon entering the trigone fuse and almost immediately bifurcate to diverge at an acute angle. The diverging nerve cords are connected by many fibers and a narrow triangular pattern results (Fig. 7). In contrast to the more frequent (35 per cent) and similar though wider triangular pattern and the relatively rare (1 per cent) spider web pattern (Fig. 8) which is found when the divergence is marked and the connecting fibers are numerous and fine. In only 3 dissections (1 per cent) were arch shaped patterns encountered (Fig. 9).

The plexus may be shifted so as to occupy position solely to the left of the midline (Figs. 10 and 11). However the infrequency (8 per cent) of

the occurrence of this left-sided shift certainly makes unacceptable Reynolds' statement that "the nerves which comprise the so called hypogastric nerve pass caudally a little to the left of the midline. These left-sided plexuses were frequently found to be immediately adjacent to the left common iliac artery and the root of the sigmoid mesocolon. This is of considerable surgical interest since the extirpation of the retroperitoneal fibro-adipose tissue in the central portion of the interiliac trigone would fail to remove the nerve fibers constituting this type of plexus. An appreciation of the foregoing fact and that a single "presacral" nerve rarely exists—that the superior hypogastric plexus is always prelumbar and frequently occupies the entire interiliac trigone will cause fewer failures to be reported after superior hypogastric plexus sympathectomy. The incomplete extirpation of the plexus, the improper selection of cases and to a lesser extent the occurrence of neuromas in the remaining nerve stumps being the chief causes of poor results in surgery of the superior hypogastric plexus.

In 8 per cent of the subjects the intermesenteric nerves continued into the trigone as multiple parallel bands, frequently fusing just before reaching the promontory of the sacrum to form the inferior hypogastric nerves. These multiple parallel cords or bands were connected by many fibers.

After consideration of the large variety of patterns and the variations within each pattern group one can well endorse the statement: "It is difficult to find two plexuses with the same anatomical architecture" (Labate).

SURGICAL ANATOMY

A consideration of the surgical anatomy of the superior hypogastric plexus necessitates an appreciation of (1) the interiliac trigone in which the fibers of the plexus are always found (2) the normal contents of the trigone (3) abnormal contents of the trigone and finally (4) the variations in the pelvic mesocolon.

The interiliac trigone has for its apex the bifurcation of the abdominal aorta, its lateral boundaries the common iliac arteries, and its base corresponds to a line joining the two common iliac arteries at the level of the promontory of the sacrum. The trigone therefore embraces an area comprising the lower half or third of the fourth lumbar vertebra, the intervening intervertebral cartilaginous disc and the fifth lumbar vertebra. Its length varies with the level of bifurcation of the abdominal aorta and averages approximately 6 centimeters (4.9 cm. to 6.4 cm.). It tends to be slightly more elongated in the male (by approxi-

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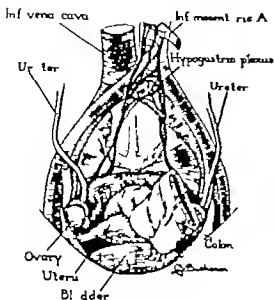


Fig. 2.

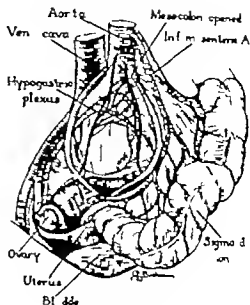


Fig. 3.

the sigmoid mesocolon and are distributed to the sigmoid. As they enter the root of the pelvic mesocolon they lie on the left border of the interiliac trigone and in instances in which a type III mesocolon exists they assume importance in superior hypogastric sympathectomy since it is necessary to dissect between the layers of the mesocolon to expose the interiliac trigone, and in such a dissection these vessels may be injured.

The interiliac trigone is entirely retroperitoneal. Its peritoneal covering on the right is reflected to the lateral walls of the pelvis and spreads downward to the anterior surface of the sacrum. On the left the peritoneum descends from the abdomen to the rim of the pelvis where it is reflected over the sigmoid colon and the upper portion of the rectum whence it is again reflected to the inner aspect of the anterior abdominal wall. The peritoneal layers which have thus ensheathed the pelvic colon approach each other superomedially and fuse to form a true mesentery the pelvic mesocolon. Between the two layers of the pelvic mesocolon run the vascular and nervous supply of that section of the bowel.

There is considerable variation in the length and the position of the line of attachment of the pelvic mesocolon. In general three main types may be described.

Type I. A short mesocolon easily retracted to the left and allowing adequate exposure of the interiliac trigone (Fig. 13).

Type II. A long mesocolon which may readily be shifted or retracted to expose the interiliac trigone (Fig. 14).

Type III. A long mesocolon, the leaves of which embrace the interiliac trigone, its attachment being along the midline. This type of mesocolon makes difficult the exposure of the interiliac trigone, particularly when dissection between the leaves of the mesocolon is resorted to in order to expose the superior hypogastric plexus (Fig. 15). This type of dissection endangers the vascular and nervous supply which is transmitted through the mesocolon to the bowel it ensheathes. Dissection between the layers of the mesocolon should be avoided and the superior hypogastric plexus exposed by incision parallel to the root of the mesocolon and through both of its layers (Eliot). In a series of 50 dissections Eliot reported the occurrence of 78 per cent of the first type of mesocolon, 14 per cent of the second, and 8 per cent of the third. Roussel reported type III mesocolon in 15 per cent of his cases, while Cotte found it in only 2 per cent. Bernard and Theodoresco and Labate have each reported its occurrence in 1 case.

In this series in females type I occurred in 75 per cent, type II in 25 per cent. Type III did not occur. The incidence was similar in the negro and the white. However in males there was a greater occurrence of the type III mesocolon in the negro, the percentages being 8 of type I, 14 type II, and

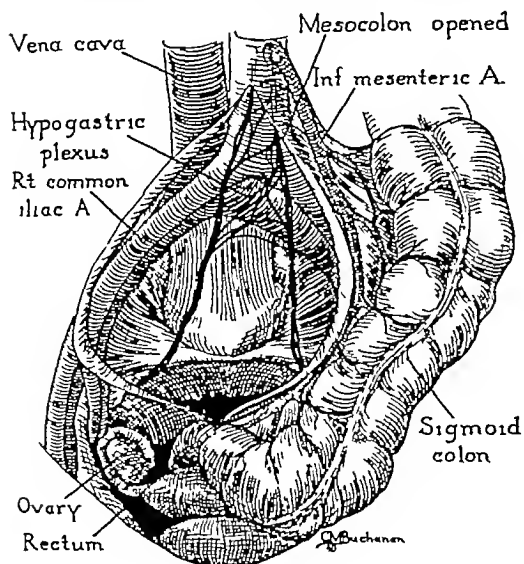


Fig 14

5 type III in the white, while they were 70 type I, 16 type II, and 14 type III in the negro. As previously noted this was the only significant racial difference encountered.

In addition to these normal relations of the interiliac trigone, various anomalies have been encountered. In 4 dissections accessory ureters were found which traversed the trigone. Davis similarly reported occurrences of accessory ureters in 3 of the 12 operative cases he studied. In several of our dissections in the infant, the right ureter bent rather sharply toward the midline and so was included in the trigone and subject to injury. This finding is confirmed by Labate, who included 52 infants in his report of 75 dissections.

In 3 of our dissections the transverse duodenum was found anterior to the interiliac trigone. In 1 of these cases the other abdominal viscera were also ptosed. In the 2 others the abdominal viscera were normally located with the exception of the duodenum. The left common iliac vein in 14 per cent of our dissections had sharp S-like deviations toward the midline, and projected into the interiliac trigone to well beyond the midline occupying the entire upper and left half of the trigone. In 2 per cent of this series the left common iliac artery had a similar deviation, and occupied a position which would normally be well within the interiliac area. In these 2 instances the artery was partially covered anteriorly with the hypogastric plexus which in each of these instances was of the spider-web pattern, and occupied an area comparable to the normal trigonal area. In

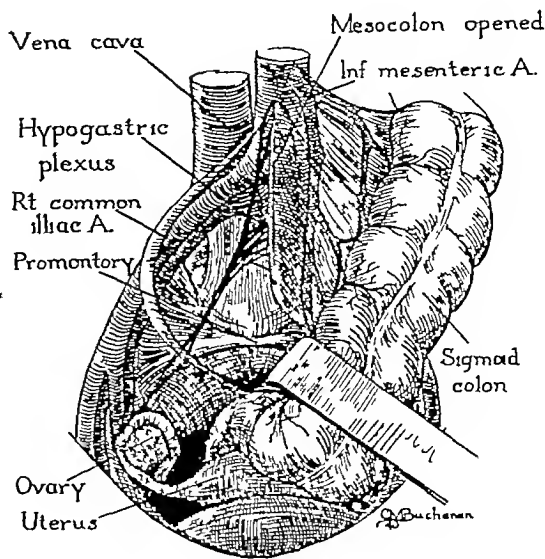


Fig 15

1 subject the right and left common iliac veins joined to form the inferior vena cava anterior to the bifurcation of the abdominal aorta. The interiliac trigone in this instance was bounded by the vena cava superiorly and the common iliac veins laterally, the aorta and common iliac arteries being posterior to these structures. The superior hypogastric plexus in this instance was of the multiple cord pattern and within the venous triangle.

The discussion of a very important vascular anomaly which occurs with surprising frequency and which has gained little attention in the literature has been left for last. The majority of investigators are silent on the subject. Elaut states "One must bear in mind a certain anomaly of the blood vessels occurring not infrequently within the interiliac trigone. In our rather small series of cases we met this condition twice, namely a large, pencil-sized vein arose from the left common iliac vein, proceeded directly across the trigone and joined the opposite wall of the pelvis at a spot close to the bifurcation of the common artery. The veins lay on the periosteum, the nerves cross it obliquely, being adherent in a few places." In the series of dissections herein reported anomalous veins of this type were found 26 times! Seventeen occurred in the male, and 9 in the female, with the distribution even between the negro and white. In several instances the vein was half as large as the common iliac vein, while in the greater number of cases the vein was of much smaller size. In 3 instances these large veins arose within the substance of the psoas

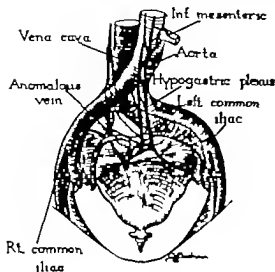


Fig. 6.

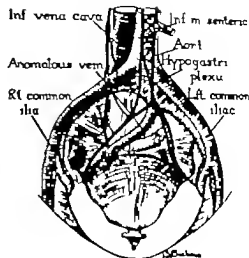


Fig. 7

muscle on the opposite side of the pelvis and crossed the interiliac trigone to empty into the left common iliac vein. Many of the smaller veins could be traced directly from the peritoneum traversing the interiliac trigone and emptying into the common iliac vein. Several of the veins were in the nature of accessory hemorrhoidal veins which ran retroperitoneally to the left of the midline in the interiliac trigone to empty into the left common iliac vein. These veins are a distinct surgical hazard, and should be given much greater emphasis. Further investigations of their exact origins are in progress (Figs. 16-17).

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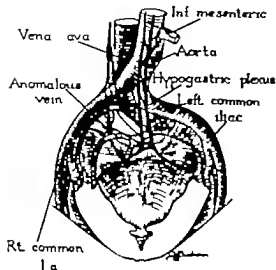


Fig. 6.

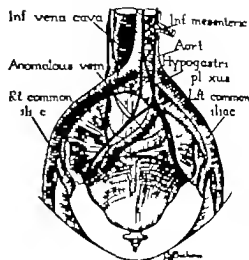


Fig. 7

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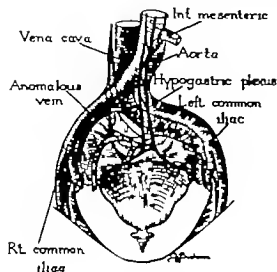


Fig. 16.

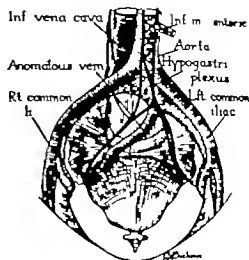


Fig. 17

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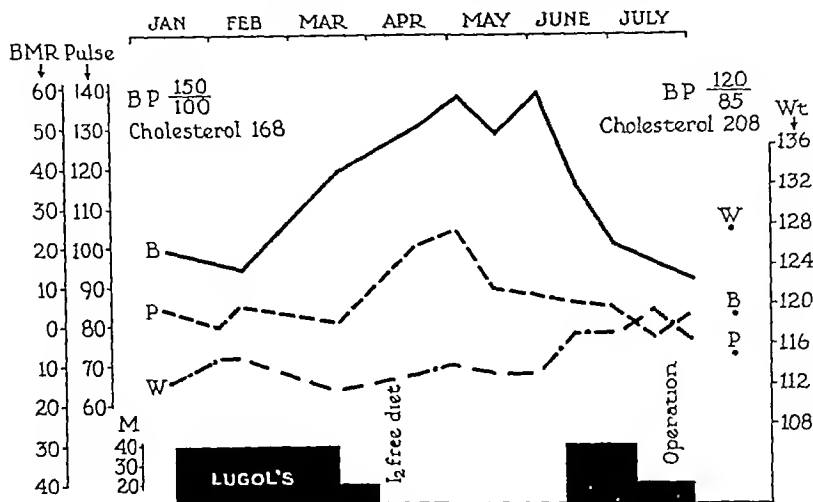


Fig 2 Case 2

ically," the only *safe* way to treat that patient further is to take him off iodine *gradually*. Then after a period of time, say 2 to 4 months, when the thyroid will again respond the patient can be operated upon safely under its influence.

With this in mind, we suggest the following regimen to be used in such cases. When it is obvious that a patient will not have an "iodine remission" he is weaned from it, so to speak, that is, the iodine is stopped gradually so that a crisis will not occur. The weaning process may take a few days or it may take weeks. The symptoms may become slightly aggravated but

bed rest and sedation have been found ample to control them. The x-ray may also be helpful. Second, the patient is placed on an iodine-free, or low in iodine, diet but high in proteins, vitamins, and carbohydrates. It must be emphasized again and again to the patient not to take iodine or any foods containing it and to take no medicine other than that prescribed. The patient may be seen at weekly intervals for the first month or so and then every month until sufficient time has passed, 2 to 4 months. At the end of this time he is again hospitalized and prepared in the usual manner for operation.

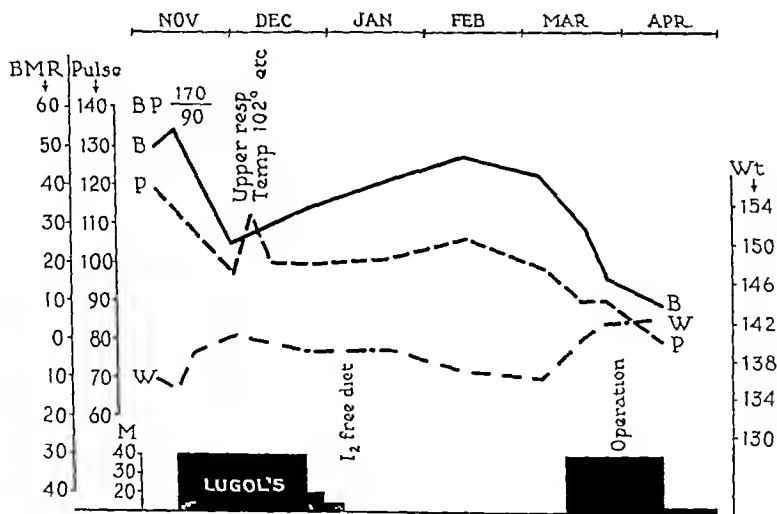


Fig 3 Case 3

SO CALLED "IODINE RESISTANT" HYPERTHYROIDISM

J. E. KEARNS, J. M.D. F.A.C.S., and PAUL STARR, M.D. Chicago, Illinois

THE operative mortality rate in well controlled cases of hyperthyroidism is still between 1 and 5 per cent depending upon the co-ordination between the medical and surgical divisions and the number of severely ill patients included in the series studied. We do not consider the patient with Graves disease an emergency until he has been started on iodine even the acutely ill patient can be controlled for a period of time with diligent medical and roentgen therapy. A few cases of toxic goiter between 5 and 10 per cent, will not respond to the usual preoperative iodine therapy and some appear to become definitely worse with its use. These patients are usually in the older age group and it is our opinion as well as that of others, that the mortality and morbidity following operation in these cases are higher.

We wish to show that these so called "iodine resistant" or "iodine fast" cases will respond to a specific regimen of therapy that they are not emergency cases, but that with time they can be operated upon under the influence of iodine. Blank, Means, and others have definitely found, both by clinical and pathological studies, that

some of these patients are in reality being controlled by iodine. There is no clinical evidence of this fact, however because the use of the iodine is preventing a crisis. Crisis, in itself, would suggest that great caution should be exercised in anticipating operation at this time.

A search of the literature reveals that this condition was not described until after Marine and Kimball in 1917 advocated the use of iodine and iodized salt in the prevention of "endemic goiter" and when Plummer and his associates recommended in 1923 the use of Lugol's solution in the preoperative and postoperative care of toxic patients. It is obvious to us that some of these patients have been taking sufficient iodine so long that the thyroid is no longer able to respond to its use. The source of the iodine may be salt, food, old family remedies, or patent medicine. W. O. Thompson et al. have shown that the minimal effective dose of compound solution of iodine varies between 6 and 10 milligrams a day. The average person consumes about 1.5 milligrams of iodine a day in table salt alone without considering other food sources. It is a well known fact that if a patient has been receiving Lugol's solution or some other iodine substance for a long time in an attempt to manage his condition "med-

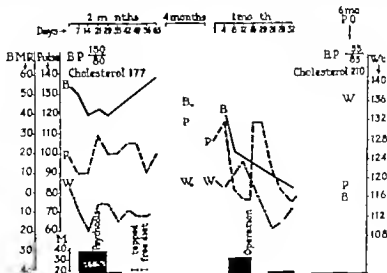


Fig Case
56

HAZARDS OF FIRE AND EXPLOSION OF ANESTHETIC AGENTS

II In the Presence of the Cautery

BARNETT A. GREENE, M.D., Brooklyn, New York

WE have described, in a preceding report,¹ the hazard of anesthetic combustion during the use of x-ray apparatus. Like x-ray equipment, the cautery is a common source of danger that is always condemned by writers on anesthetic explosions but without sufficient explanatory detail to force every anesthetist and surgeon to realize how serious is the danger and how great is the need for accurate and minute knowledge of the facts of anesthetic combustions. In this paper we deal at length with the information required of the anesthetist and the surgeon which will enable them to use the actual cautery safely and yet without unnecessary restrictions.

We also discuss here, because it is most fitting, ignition by such obviously hot objects as the cautery, gas flame, match light, or cigarette, also mentioned are the small group of fires caused by the application of the cautery to surgical fields prepared with ethyl chloride spray anesthesia, or with inflammable skin cleansers like ether or alcohol, or with inflammable skin antiseptics like the various tinctures.

The actual cautery is an important surgical instrument employed in almost every operating room at least several times a week. Familiarity with the cautery has bred contempt for this hazard. On the other hand, unreasonable restrictions against the use of the cautery should not be placed in the way of the surgeon desiring to employ it.

Why have there been at least 55 known and wholly preventable anesthetic fires and explosions ignited by such an obvious hazard as a cautery, flame, or other hot object? We think the explanation is to be sought in the following reasons:

1 Ignorance of an elementary knowledge of anesthetic combustion. Our personal survey has

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¹This is the second of a series of papers on the explosion and fire hazard of anesthesia based on a study of the literature and of the case reports secured by the Committee on Anesthetic Hazards. Dr. Barnett A. Greene, chairman, this group acting as a subcommittee of the Research Committee of The American Society of Anesthetists, Inc.

found an astonishingly large number of surgeons and anesthetists who lack basic and even rudimentary information on this subject.

2 Indifference toward the hazard because of past good fortune while using set-ups in the operating room which we consider dangerous.

3 A paucity and inflexibility of anesthetic methods available to many surgeons who must use the cautery. (*This is the usual reason for the use of hazardous techniques*.)

In short, the cause is almost always ignorance. The cure must be education and elevation of the standards of anesthetic training and practice.

PHYSICAL AND CHEMICAL DATA

The fundamental physical and chemical data included in the first report (22) will not be repeated, although they should be familiar to all who read this and subsequent reports. We shall, however, present such supplementary facts as have a special bearing on the particular type of hazard under discussion.

The following information, added to the basic scientific facts presented in our first paper, should be required knowledge of every anesthetist, and also of every surgeon who desires or is obliged to dictate the choice of anesthetic procedures.

1 The minimum ignition temperatures at 0 degrees C are shown in Table I.

TABLE I—MINIMUM IGNITION TEMPERATURES

	In air	In oxygen
Diethyl ether	304	182
Dimethyl ether	399	327
Ethylene	490	485
Cyclopropane	498	
Ethyl chloride	517	468

It is apparent that the presence of a high concentration of oxygen instead of air (21 per cent oxygen and 79 per cent nitrogen) lowers the minimum ignition temperature of a combustible agent, nitrous oxide lowers it even more than does oxygen (8).

As shown in Table I ether-oxygen and ether-air mixtures are more easily ignited than similar mixtures of ethylene or cyclopropane.

Brief reviews of 3 cases with their clinical records are presented to show the efficacy of this method. A third case is presented to demonstrate the value of the method in a patient who developed a preoperative complication that made postponement of surgery to a more opportune time necessary.

CASE 1. Mrs. H. H., 50 years of age, sought relief for palpitation, loss of weight, nervousness (hysteria at times), heat intolerance, and eye trouble. There was no history of iodine medication for years. Physical examination showed nervous, acutely ill female pulse, 90 blood pressure, 80/80. The skin was hot and moist. Ith definite pigmentation over the forearms. She presented moderate exophthalmos and had numerous eye signs. A firm thyroid was palpable, but there was no bruit. Laboratory reports were essentially normal except for metabolic rate of plus 54 per cent. From study of the chart (Fig. 1) it can be seen that on Mrs. H.'s first admission to the hospital there was little, if any, response to 25 days of iodine therapy so this was stopped gradually and the patient was discharged from the hospital. Four months later she was readmitted to the hospital and was operated upon successfully following an iodine remission. It is interesting to note the postoperative reaction following the abrupt withdrawal of iodine and its subsidence when iodine was started again.

CASE 2. Mrs. A. G., 46 years of age, also had rather typical history and findings of toxic goiter. Ith no previous story of iodine medication. The physical findings showed nervous, well developed, white female pulse, 95 blood pressure, 58/70. The thyroid was enlarged, with slight bruit, firm, and nodular. In this patient's clinical course (Fig. 2) she was one of the few that have seen who developed more severe toxic symptoms while on iodine,

but after period of 13½ months without it were able to secure remission and she was safely operated upon.

CASE 3. Mrs. J. F., aged 30 years (Fig. 3) presented clinical symptoms and findings of Graves' disease. She developed an acute upper respiratory infection on the 11th day of preoperative preparation, and had escaped from the iodine effect by the time this was controlled. The patient was sent home on an iodine free diet, etc. for 3 months and has since been readmitted to the hospital and successfully operated upon.

CONCLUSION

The 3 cases presented show the benefit of the conservative handling of so called iodine resistant cases as well as in one in which postponement of operation was necessary.

We realize the difficulty of managing these patients unless they can be kept under constant observation but do believe that in cases not emergencies, the type of care described will result in a further reduction in mortality and morbidity.

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may safely apply the cautery in the region of the head after an inflammable anesthetic mixture has been administered. This situation, expected or unexpected, is frequently encountered. Many case reports testify to the incorrect answer to the question and record the consequent death of the patient.

The duration of the period in which an etherized patient exhales an inflammable concentration after the administration of ether has ceased depends on the minute-volume of respirations and the degree of saturation of the patient with ether. The expired breath of a patient in third stage anesthesia immediately after the end of administration of ether-air, ether-oxygen or ether-nitrous oxide-oxygen is probably combustible. This may be inferred from the data of anesthetic concentrations compared with the figures for explosive concentrations, for the concentration of ether for the induction and maintenance of anesthesia is at least 2.5 per cent, more often 3.5-4.5 per cent (1), and the lower limit of inflammability of ether in air is 1.85 and of ether in oxygen is 2.10 (21). Furthermore, as long as the patient remains in full surgical anesthesia we might expect to find an inflammable percentage of ether in the breath. This deduction is based on the data quoted by Beecher from the research work on dogs by Haggard and Robbins (1). They have shown that surgical ether anesthesia is induced and maintained with 3.7-4.5 per cent ether in the respired air, that this produces a blood ether concentration of 100-120 milligrams per 100 cubic centimeters of blood, and that light (first plane) surgical anesthesia corresponds with an arterial blood ether content of 115 milligrams per 100 cubic centimeters (1).

These inferences are contradicted (a) by the statement of Hewer that "the exhalations of an etherized patient are probably never inflammable or explosive" (10), and by (b) the report of Hasler (17) that samples of air taken at a distance of 2 inches from an open mask, after an operation had been in progress for an hour and 10 ounces of ether had been used, were noncombustible, and (c) by the work of Featherstone and Morgan (6, 27) who were unable to ignite, by spark or flame (1) specimens of expired air and ether collected immediately after the withdrawal of a heavily impregnated ether mask, (2) collected expirations during deep ether anesthesia, or (3) a mixture exhaled immediately after a deep inspiration of a strong ether air mixture.

Despite these negative and reassuring reports we must take a skeptical attitude because in addition to the danger theoretically inferred from explosive and anesthetic concentrations, we possess

case reports which testify to the reality of the danger. Even Featherstone is not sure of the safety of his findings as indicated by his advice that the patient under ether should be allowed to take a dozen breaths of fresh air after the administration of ether has ceased (9). We feel, however, that such a practice is too unreliable (because the rate of exhalation of ether may be very variable) on which to depend for an act so hazardous as applying a cautery in or near the head of a patient who has had ether.

To resolve the inevitable doubt at a time when it is urgent and important to know positively whether or not the expirations of a patient are inflammable, we recommend the simple method suggested by Flagg (10). He has advised the withdrawal of a sample of the expired pharyngeal air by means of a bulb syringe and the testing of the inflammability of its contents in an adjoining room by emptying the syringe across an alcohol lamp flame. An inflammable mixture changes the color of the flame by taking fire, an explosive mixture harmlessly "pops." In place of the 2 inch rubber bulb fitted with the glass top of an eye dropper which Flagg has used, we prefer, as safer and simpler, an all-rubber ear syringe of the same size. There is no possibility then of shattering glass or of the glass top slipping out of the bulb handle. This test is simple, safe, and positive in its results. If the test, which we shall hereafter refer to as the Flagg test, is negative then "the field is absolutely safe for cauterization at that time" (10).

An important fact, related to the safety of using a cautery near the head of an etherized patient, is that the stomach may contain an inflammable concentration of the anesthetic swallowed during induction. This is much more likely with ethylene and cyclopropane than with ether (which is administered in concentrations not much above the minimal limit). The stomach bubble of combustible gases may be regurgitated during the period when the patient is breathing fresh air and is ascending from surgical anesthesia. At this critical moment the cautery might be applied in or near the head of the patient. Thus there might occur an explosion under conditions considered safe because the patient had been allowed to take a dozen breaths of fresh air and the Flagg test had been found negative only a few seconds or a minute before. Therefore if an igniting agent such as a cautery or hot metal dental syringe must be used in the upper respiratory tract after the patient has received a combustible anesthetic it is necessary to deflate the stomach by intubation before securing a negative Flagg test.

The minimum ignition temperatures of liquid ether and mixtures of ether with air oxygen or nitrous oxide are well below visible spark temperatures (3, 4, 13). Kirby Thomas has found that certain mixtures of ether-air or ether-oxygen can be exploded at temperatures below 100 degrees C. (33).

The hot element of all cauteries can ignite any combustible anesthetic mixture. Many case reports have demonstrated this fact beyond doubt.

2. Electric cauteries present four points at which igniting temperatures may be produced: (a) the heated element, (b) the foot pedal switch, (c) the rheostat, and (d) the cord or terminals which may break because of frequent usage or become detached because of inadvertent pulling (39) thus producing sparking.

3. A knowledge of the densities of anesthetic gases and vapors is important in understanding the cautery hazard. As compared with air having a density of 1 ethylene has a density of 0.97, cyclopropane .45 ethyl chloride, .73 divinyl ether, .745 and diethyl ether .56 (2).

The rate at which a gas or vapor will diffuse or mix with air is inversely proportional to the square root of its density (rate of diffusion $\propto \frac{1}{\sqrt{\text{Density}}}$).

for this reason anesthetics having low density such as ethylene will diffuse more rapidly into air than will ether vapor. This means that rich mixtures of ethylene on being discharged into an operating room will pass through the explosion range and become nonexplosive, other conditions being constant, sooner than a heavy vapor. A heavy vapor such as ether has a tendency to remain longer in its highly concentrated condition and on account of its greater density will tend to descend and accumulate at the floor level and under favorable circumstances may flow a considerable distance from the source of discharge. On account of these characteristics, the fire hazards are greater for vapors of this type. (31) Ether has been known to take fire at a measured distance of 5 feet from the source of escaping vapor (34).

It is because of its heavy density as well as its frequent administration in open techniques that we find ether to be the most often ignited anesthetic when the igniting agent is external to the anesthetic circuit, e.g. cautery faulty electrical apparatus, and flames.

The actual concentrations of ethylene in the atmosphere of operating rooms has been well studied by Cheney and Folkman. Based on several thousand readings made in 4 hospitals of modern construction but without unusual ventilating sys-

tems, the conclusions of their report are worth repeating here (4).

"a. At distances of 10 feet or more from the patient's head the concentrations were so small as to be indeterminable.

"b. No evidence of accumulation of ethylene percentages in any part of the operating room was found after the longest period of continuous anesthesia (with the partial rebreathing method of administration).

"c. Electric switches on the walls of the operating room were shown to be entirely harmless inasmuch as the maximum ethylene concentration at these points was less than 0.1 per cent.

"d. The only points where explosive concentrations of ethylene occurred were in the immediate vicinity of the face mask. The dangerous area extended to 1 foot above the face mask and 3 feet to the particular side of the mask toward which the expiratory vent pointed. Immediately to the side of the mask but on the side opposite that toward which the vent was directed the ethylene concentration was less than . . . per cent.

"e. With the vent of the exhalation valve pointed to the side, no concentration above the chest of the patient was found higher than 0.3 per cent in those cases in which the anesthetist used a cloth shield between the field of operation and the patient's head. These percentages were also reduced when the anesthetist used rebreathing.

"f. With the use of a cloth shield, proper adjustment of the exhaling vent and the technique employed by the anesthetist during these tests, it would appear that the cautery could be used in the abdomen with entire safety. (The technique used in these tests included a tightly fitting mask, exhalation vent directed to the side and not straight up and, most important, a large percent age of rebreathing.)

Since the time of these studies (1930) the method of complete rebreathing has become standard practice. With this method the atmosphere of the operating room is more likely to be free of an explosive concentration of ethylene or any other anesthetic, even in the region close to the mask. But sudden, unexpected breaks in the closed circuit because of vomiting, the need to use suction or to insert an airway preclude the possible use of the cautery or a flame near the head, neck, shoulders and chest, even with a perfectly closed circuit (a theoretical assumption that is frequently not attained in clinical practice).

4. Exact information on the combustibility of the expirations of a patient under anesthesia and the duration of its inflammable status is needed to enable the anesthetist to know when the surgeon

the patient, the type of surgery, or the limited experience and ability of the available anesthetist), then the following conditions should exist before the cautery is switched on

a A meticulously closed circuit method of administration should have been in use during the prior 10 minutes, an arbitrary but clinically determined safe period (13)

b The combustible anesthetic of choice, if combustible it must be, is ether-air by closed circuit administration because of its smaller tendency toward propagation and smaller range of explosibility as compared with ether, ethylene, or cyclopropane mixtures with high concentrations of oxygen or nitrous oxide Cyclopropane, ethylene and ether with oxygen are permissible, however

c The ventilation should have been arranged to increase the dispersion of anesthetic gases and vapors previously allowed into the atmosphere The direction of ventilation should be away from the cautery and toward the patient's head

d The patient should be securely set in third stage anesthesia (deep first plane or deeper) to be certain that no vomiting occurs to break the closed circuit during the period of cauterization

e No part of the cautery, its wires, switch, or rheostat should be near the anesthetic apparatus

f A draped screen should be placed so that it will intervene between the head of the patient and the field of operation

g If doubt exists as to the freedom of the room from inflammable concentrations of anesthetics released into the air before the circuit of anesthetic administration is closed, then a "Flag test" should be applied to the possible points of contact of the cautery apparatus with atmosphere

5 If the cautery is to be used on or in a hollow viscus in the abdomen, such as the bladder or stomach in addition to the precautions listed in paragraph 4, we advise, when ethylene, cyclopropane or acetylene is used, that one take pains to empty the viscus of its gaseous content just before the cautery is applied (13)

6 If the cautery is unexpectedly required in a case which has been inhaling a combustible anesthetic, the necessary precautions before the cautery is permitted are

7 If the field of operation is on or in the head, neck, chest or respiratory tract, the anesthetic should be changed to another but noncombustible type while the respiratory tract is ventilated with air and the stomach is emptied until the Flag test is negative both at the field of operation and the atmosphere adjoining the cautery apparatus at any of its parts

TABLE II—SUMMARY OF 55 CASES

Agent	Total no of cases	Cautery or flame used near head neck chest etc.			Cautery or flame used in abdomen or elsewhere		
		No of cases	Deaths	Injured	No of cases	Deaths	Injured
Ether air	12	3	1	2	2	0	2
Ether-O ₂ (with or without nitrous oxide)	17	7	4	5	5	0	3
Ether air or O ₂	6 [§]						
Ethylene	9	6	5	4	4	0	3
Ether or ethylene or both	1	1	1				
Ethyl chloride	3				3	0	2
Acetylene	3				2	0	2
Cyclopropane	2 [§]						
Alcohol		1	0	1	1	0	1

*The cases counted in this group are only those in which the presence or absence of injury is known
 †The total number of persons injured or killed is stated in some instances more than one person was injured In no case was more than one person killed
 ‡One patient died—classification not possible for want of details of explosion

b If the field of operation is on or in the abdomen, pelvis, perineum, lumbar back, and extremities, the anesthetic may be continued with a closed circuit administration together with the precautions advised in paragraph 4 or the anesthetic may be changed to a noncombustible type with the precautions which are advised in paragraph 6a

In the event of the situations described in either paragraphs 6a or 6b, proper ventilation away from the cautery and toward the head of the patient should be arranged

We realize that these rules of conduct appear complicated, but they really are not any more than a detailed description and summation of modern anesthetic procedure as practiced by many leading anesthesiologists, and required of all who wish to avoid any of the accidents known to have occurred

This description is an elaboration of the knowledge which Guedel assumes when he states the factors determining the use of the cautery in the presence of an inflammable agent as "appreciation of the weight of the vapor, the distance of this from the cautery, the amount of vapor freed into the room and the direction of air currents The only unusual precaution we have added is the Flag test which should be more widely and frequently employed to substitute proof of safety for guesswork Of course, the simplest and ideal

The respiratory tract of a patient in third stage anesthesia under ethylene-oxygen probably does not contain an explosive mixture because the concentration of ethylene is in the range of 85 to 90 per cent whereas the upper limit of explosive concentrations of ethylene in oxygen is 79.9 per cent (21). Within a few breaths of air or oxygen, however, the explosive range is reached. The exhalations of a patient under cyclopropane oxygen are always inflammable just as is true of ether because the anesthesia concentrations are always in the inflammable range. As to how long the respiratory tract contains an inflammable mixture after the cessation of administration of ethylene or cyclopropane there are no definite data but one should apply all the precautions advised here for ether: namely the breathing of fresh air the use of the Flagg test, and intubation of the stomach.

The preceding discussion of facts, which might be of value when the cautery is to be used in or near the head of a patient who has received a combustible anesthetic, should not be interpreted to mean that we believe this to be good practice. When any igniting agent is to be employed in such a dangerous location it is far safer and it is our invariable rule, to use a noncombustible anesthetic technique. But there have been and will be many instances when, after an inflammable anesthetic has been given the surgeon is suddenly and unexpectedly required to use a cautery fulguration, coagulation, etc. In such circumstances, the information which is given here will prove to be invaluable.

CLINICAL DATA

Most writers flatly object to any use of the cautery in the presence of combustible anesthetics. Others have employed the cautery with only few precautions. For example, Horsley (20) has reported using the cautery in 4 of his first 116 anesthetics with ethylene-oxygen with only partial rebreathing without any trouble although care is always taken to increase the operating room ventilation temporarily while the cautery is being used and the cautery is never used near the mask nor in operations on the head or neck. Yandell Henderson (8) has stated the use of the cautery in the abdomen (with ethylene and partial rebreathing) is safe only when a screen or curtain is placed between it and the patient's face. Personal communications from many surgeons of long experience have described the long and uneventful use of ether by open drop or partial rebreathing administration during cauterization in the abdomen, pelvis, and perineum. It is to be expected that those who practice or allow the

practice of anesthesia with carelessness, or who are ignorant of its hazards are not likely to submit reports to the literature or scientific societies and therefore, just those in greatest need of criticism and correction avoid them.

On one point all authorities are agreed. Under no circumstances can any cautery or other spark producing equipment be used around the head of the patient or the pleural cavity, when the patient has been anesthetized with any inflammable anesthetic. To do so is criminal negligence (20). Despite this unanimity of opinion, we have been able to find in at least 26 of the 55 cases of combustion reported in this paper due to the cautery and flame that the igniting agent was used under conditions which would be considered today to be criminally negligent.

Many authorities realize that it is not practicable to prohibit any and all use of the cautery in the presence of a combustible anesthetic (27, 30). A large number of leading anesthesiologists have admitted using cyclopropane, ethylene, or ether by closed circuit administration during the application of a cautery in abdominal operative procedures (5).

It is imperative that we formulate what we consider a safe and practicable set of principles governing the use of the cautery in the operating room. After a study of the physical and chemical data published and unpublished reports of others and as a result of his own experiences, observations, and discussions with leading anesthesiologists, the writer has formed the following opinion:

1 The anesthesiologist should specifically inquire before the start of the anesthesia as to the possible use of the cautery.

If the cautery must be used on or in the head, neck, shoulder, chest, respiratory passages or pleural cavity the anesthetic must be of a noncombustible type (e.g. regional block, nitrous oxide intra venous barbiturate or rectal basal anesthesia or combinations of two or more of these). The use of chloroform is to be avoided because it is decomposed by heat to form irritating fumes (30).

3 If the cautery must be used in the abdomen, pelvis, perineum, lumbar back, lower extremities or distal parts of the upper extremities, the anesthetic of choice should be of a noncombustible type provided it is as safe, from all other viewpoints, for the patient as would be the combustible inhalation anesthetic that would have been chosen had the surgeon not used the cautery.

4 If the cautery must be used in those regions listed in paragraph 3 and a combustible anesthetic must be administered because of the condition of

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precaution against explosions is to avoid all combustible anesthetics when the cautery or flame must be used in the operating room. The more experienced and versatile the anesthetist the more often is the ideal precaution practiced. But we must remember that many circumstances associated with the surgeon, patient, or anesthetist prevent the use of a noncombustible anesthetic everywhere and every time a cautery is employed.

CASE REPORTS

We possess the records of 55 cases of anesthetic ignition by a cautery flame, or similar hot object (Table II). These include all that were obtained by circularizing the members of the American Society of Anesthetists and by intensive searching of the literature. They are only a small fraction of the total number of such accidents of which the very great majority have remained untold for fear of criticism or litigation.

SUMMARY AND CONCLUSIONS

In this paper the second of a series of reports on anesthetic combustion hazards, we have presented the physical, chemical and clinical data required for an adequate understanding of the dangers and the safeguards associated with the presence of a cautery or flame in the operating room.

2. Fifty-five anesthetic (and related) fires and explosions ignited by a cautery or flame have been collected. These are all the cases we could find after a survey of the literature and extensive questioning of members of The American Society of Anesthetists, Inc.

3. In at least 26 cases, the cautery or flame was present in or near the head, neck, chest, and respiratory tract of the patient and in all of the other cases the cautery or flame was incorrectly or inadequately protected from contact with a combustible agent.

4. In no instance was there a really closed circuit of administration although in several instances there were attempts to secure complete rebreathing for cauterization about the head and the anesthetists involved believed the circuits to be tightly closed.

5. Tabulation of the 55 cases presented in this report clearly shows the truth of the following statements:

a. Explosions and fires of all combustible anesthetic agents and mixtures are capable of causing death.

b. Explosions of ether-air mixtures are capable of causing death.

c. Ether-air mixtures have a relatively small tendency toward propagating a wave of flame or pressure into and down the respiratory tract.

d. Ether-oxygen, with or without nitrous oxide, has the same great tendency toward propagating a wave of flame or pressure through the respiratory tract as has ethylene-oxygen and cyclopropane oxygen when compared under similar clinical circumstances, i.e., the location of the point of ignition with reference to the respiratory tract of the patient.

e. In no case of which we have satisfactory knowledge has anyone been killed when the cautery or flame was present outside of a 12 inch zone surrounding the upper respiratory tract. This is just as true of ethylene as it is of ether. The large admixture of air (79 per cent nitrogen) which is inevitable when the inhalant anesthetic is ignited at a distance of 12 inches or more markedly diminishes the great explosive force and propagation tendency of combustible mixtures containing high oxygen percentages.

f. All deaths—and all were patients—have been the result of a flame or cautery employed within a 12-inch danger zone surrounding the upper respiratory tract.

6. The Flagg test for the determination of the combustible nature of the atmosphere over or in a proposed field of use of the cautery has been described and recommended.

7. A set of rules for the use of the cautery in relation to combustible anesthetics has been outlined and proposed for the standardization of safe practice.

8. If the cautery must be used in or near the head, neck, shoulders, chest, and proximal parts of the upper extremities, the anesthetic agent must be noncombustible.

9. If the cautery must be used in other parts of the body or operating room the anesthetic agent of choice should be noncombustible. If it must be combustible then the safeguards described should be followed to the smallest detail.

10. The cause of anesthetic explosions and fires when ignited by a cautery or flame is ignorance or carelessness. The prevention depends entirely on education and the elevation of the standards of anesthetic training and practice.

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*We have just learned of three cases, never reported before, in which the patients were seriously burned as a result of anesthetic combustion caused by cautery used during an ethyl chloride operation and serious smoke oxygen ether combustion for such carbocaine.

EDITORIALS

be carried out as for carcinoma situated at a higher level. Carcinoma of the cardiac end of the stomach may also be resected through the same approach and esophagogastrostomy performed. The left chest is opened preferably through the eighth rib bed, and the lower esophagus including the accompanying vagi, isolated. The phrenic nerve is pinched, and the diaphragm is opened back to the esophageal hiatus. The lesser curvature of the stomach is ligated off down to and including the gastric artery, and the greater curvature is freed to a variable extent depending on the situation of the carcinoma. If it is in the esophagus and high enough to permit, the esophagus is divided at the cardia and the distal end is invaginated, if it extends to the cardia the division is made through the adjacent stomach and the distal end turned in. If the tumor is primary in the cardiac end of the stomach, the greater curvature should be ligated off along at least its upper half and the spleen removed. The stomach is then transected well below the tumor and the distal cut end is closed. Anastomosis is then made only or of upper stomach and lower end of esophagus by approximation and suture of end of esophagus to side of stomach within the chest. The diaphragm is sutured about stomach and the chest wall is closed tightly with an intercostal mushroom catheter inserted for suction drainage.

The writer has had a personal experience with nine resections: six primary in the esophagus and three primary in the stomach. Of the six primary esophageal cases, four patients survived the operation and of the three primary gastric cases two patients survived. Of the four cases of esophageal resection through the thorax and neck one patient died eight days after operation, one is alive after seven months and two died of recurrences ten

and fourteen months, respectively, after operation. Of the five cases—two esophageal and three gastric—treated by resection and esophago-gastrostomy, one patient, an esophageal case, is alive and free from signs of recurrence three years and five months after operation and of two gastric cases both survived the operation but have been operated on too recently to judge about the likelihood of recurrence. One patient with esophageal infection as a result of the operation and one with gastric resection died from local

There is every indication that transthoracic resection will soon become the recognized form of treatment for carcinoma of the thoracic esophagus and of the cardiac end of the stomach and with early diagnosis and early operation, the results should equal those obtained in surgery for carcinoma of many other regions of the body.

DALLAS B. PHEMISTER

MYOMECTOMY

BECAUSE myomectomy is an inherently more difficult operation than hysterectomy, its performance by any but experienced gynecologists is often associated with a higher mortality. As a result, it is still generally believed to be the same dangerous operation which, like hysterectomy, it was when it was first introduced. As a further result, its present field of usefulness is deliberately limited, although actually, when comparative series are reported by the same competent surgeons, the mortality of myomectomy is no higher and is frequently lower than that of hysterectomy.

To justify its performance, the end-results of myomectomy must include anatomical restoration, symptomatic relief and functional cure. To achieve these results, a very careful selection of cases is necessary.

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FEBRUARY 1942

RESECTION FOR CARCINOMA OF ESOPHAGUS

THE progress that has been made in the operative treatment of carcinoma of the esophagus and of the cardiac end of stomach involving esophagus represents one of the most rapid and striking contributions to surgery in the past four or five years. For about thirty years previously numerous attempts had been made at resection of the esophagus. The percentage of survivals following operation, however, was small and early recurrence was the rule, although the first case to be successfully resected by Torek in 1913 was free from recurrences at the time of death thirteen years later. In 1938 Garlock reported three survivals following thoracocervical resection and Marshall and Adams and the writer reported one case each of survival following transthoracic resection and esophagogastrostomy. Then began a sharp improvement in results, and a veritable wave of operating is now sweeping over the surgical centers of the country. That the un-

dertaking is a justifiable one is indicated by the reports of the *Transactions of the American Association for Thoracic Surgery* for 1941 and of Garlock.

The advancement has come about as a result of better anesthesia, better control of intrapulmonary pressure, more liberal use of blood transfusion for maintenance of the circulation and respiration, and better technique of esophagogastric anastomosis based partly on animal experiments and partly on experience in human operations.

Resection for carcinoma of the upper half of the intrathoracic esophagus may be performed through either the left chest after the method of Torek and Garlock or through the right chest after ligation of the *vena azygos* as advocated by Wookey. In either case the proximal portion of the esophagus is brought out through the neck and an esophagostomy established as low on the neck or chest as possible. If there is sufficient esophagus left at the lower end an esophagostomy is performed by making a short abdominal incision just below the xiphoid, passing a dressing forceps backward above the left lobe of the liver through the esophageal hiatus, grasping the pursestring suture of the esophageal stump and pulling it through to the surface. If inferior esophagostomy is impossible a large mushroom catheter gastrostomy may be performed. Reconstruction of the esophagus by a tube of skin from the front of the chest has been carried out by Wookey.

For operable carcinoma situated in the lower esophagus left transthoracic resection followed by esophagogastrostomy is usually feasible, but, when approximation and anastomosis cannot be attained the operation should

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higher percentage of malpositions and dystocias than occur in other pregnancies in the same age groups, and cesarean section need be performed only on absolute indications, since the myomectomy scar is somewhat less liable to rupture than the cesarean section scar.

Attention to certain technical considerations simplifies the operation and makes it more likely to produce the desired results. Preliminary curettage should be carried out routinely, to remove polyps, identify possible submucous fibroids, and rule out possible malignant processes. Absolute hemostasis is essential. It can be secured by a variety of simple devices, such as preliminary control of the uterine blood supply, and the placing of additional sutures half an inch beyond each end of each individual incision into the uterus. Care should be taken that sutures are not tied tightly enough to blanche the tissues, which would lead to ischemia and sloughing.

Judgment is required to determine whether multiple incisions or the removal of several fibroids through a single strategically placed incision is the wiser. Incisions on the posterior uterine wall should be avoided whenever possible, and careful peritonealization should be carried out if they must be employed.

There is almost no contraindication to the opening of the uterine cavity, even during pregnancy, when, if complications should develop, myomectomy can usually be performed without disturbance of the gestation.

There can be no quarrel with Victor Bonney's statement that since cure without deformity or loss of function must ever be surgery's highest ideal, myomectomy is a higher surgical achievement than hysterectomy for the inexperienced gynecologist, if for no other reason than that there is no standardized technique for its performance, as there is for hysterectomy, and the method of procedure therefore depends upon the exigencies of the individual case. Naturally, this is no contraindication to myomectomy. The patient's indisputable right to the best possible treatment for her special trouble should not be dependent upon the inability of her gynecologist to perform a certain operation because it is difficult, or his ability to perform one operation, particularly one which is mutilating in its results, better than he can perform another, particularly another operation which preserves function.

HILLIARD EVE MILLER

The single myoma is the ideal type for myomectomy although all types and combinations of types, including the submucous variety can safely be removed. Although a hundred or more tumors have been successfully removed from the same uterus, hysterectomy in such circumstances would usually be the operation of choice. Subsequent childbearing being one of the prime objects of myomectomy there is small point to the preservation of an organ the musculature of which is so damaged that pregnancy is unlikely to occur in it. Quite aside from the size and number of growths they frequently present, myomectomy is usually contraindicated in negro women because the high incidence of associated adnexal disease in this race militates against the functional result which is one of the aims of the operation. By similar reasoning, the location of myomas in the uterine horns is another contraindication to myomectomy. Pregnancy can occur after the removal of one tube and the opposite ovary or even after such ordinarily undesirable procedures as bilateral resection of the ovaries, but the majority of gynecologists doubt that plastic procedures on the resected tube are ever of great value. Degenerative changes, being usually limited to the tumor itself are not a contraindication.

The ideal age for the performance of myomectomy is from 25 to 38 years. Below that period fibroids seldom cause symptoms, and over it the preservation of function is not of great importance. The upper age limit may occasionally be exceeded if a single fibroid is found in an otherwise healthy pelvis, in the course of surgery for other conditions or if the patient insists for some reason upon the preservation of the uterus.

If these various limitations are observed myomectomy will be found applicable to perhaps 10 or 15 per cent of all the patients with

uterine fibroids seen in private practice. Proportions as high as 25 to 50 per cent, which have been reported, suggest that the indications have been unduly exceeded. For economic or other reasons the operation is seldom possible or even desirable in patients seen in public institutions.

Recurrence of the tumors is a possibility in a small proportion of cases 3 per cent is a conservative average, though higher percentages are occasionally reported. Recurrence is unlikely after the enucleation of large single tumors and most frequent after the removal of multiple small "seedling" tumors, for which, except for special reasons, myomectomy is not usually a very wise choice. The patient for whom myomectomy is proposed should always be warned of the possibility of recurrence but may with equal fairness, be told that it is unlikely.

Anatomical restoration of the uterus can usually be anticipated, the process of involution reducing it to normal size and shape within 2 or 3 months after operation, even when immediately afterward it is large and its contour is irregular. Symptomatic relief that is the correction of dysmenorrhea and the return of the periods to normal in character, frequency and amount of flow can be looked for within the same length of time in 80 per cent or more of all cases.

Myomectomy should not be undertaken for the relief of sterility until the problem has been surveyed from every possible angle and the candidate for operation should understand that no definite promises can be made as to results. The reported successes, however run as high as 33.3 per cent when the basis of computation is the number of suitable subjects, and when due allowance is made for the not inconsiderable number of women who frankly do not desire children. Subsequent pregnancies are associated with no

is a testimonial to its worth. It is unfortunate that one of the authors, Dr. Howard Ruggles, whose untimely death occurred on December 29, 1930, could not help in the preparation of this sixth edition.

The general character of the book has not been changed nor has any attempt been made to cover the entire subject completely. The subject material is presented in a concise but adequate manner and covers the entire field of roentgen diagnosis. The more recent advances in roentgen interpretation have been described and illustrated. In many instances illustrations have been replaced and new ones have been added. The only possible criticism that one could make is that the illustrations are in the positive rather than in the negative phase. This book is recommended without reservation as a text for undergraduate students, to postgraduate students in radiology, and to the medical practitioner.

CARL F. BARTH

THE third edition of Kolmer and Boerner's *Approved Laboratory Technic*¹ is practically the same as the second edition except for the addition at the end of the book of an appendix of the newer methods developed in the last few years. These methods include the Donath Landsteiner test for paroxysmal hemoglobinuria, Quick's method for quantitative determination of prothrombin, methods for the examination of semen, Sparkman's methods for urobilinogen in feces and urine used as a liver function test, Quick's method for hippuric acid in urine for liver function, Cherry and Crandall's method for serum lipase for pancreatic disease, a simplified Kolmer complement fixation test to be used in laboratories doing large numbers of tests for syphilis, the Eagle modification of the Wassermann test, a modified Medes method for vitamin C in urine and the Farmer and Abt method for plasma, the Bratton and Marshall methods for sulfanilamide in blood and urine, and sulfathiazole in blood, the hedside method of Ratish and Bullock for sulfapyridine in blood, and Barker's method for thiocyanates in blood. The only changes in the main portion of the text from the last edition are the correction of errors and the addition of two tables: one, on page 314, is by Merritt and Fremont Smith comparing normal cerebrospinal fluid with blood plasma, the other, on page 379, tabulates the color changes of the indicators of Clark, Lubs, and Cohen.

In most instances only one method is enumerated for each test, on the whole these are adequate. A uniform method of presentation of each test is conformed to throughout the book. The principle of the test is stated first, then the technique is given in outline form making it easy to follow. A praiseworthy feature in many of the procedures is the statement of the sources of error. A large number of the methods have a brief discussion of the interpretation or sig-

nificance of the results of the test. However, this is not adequate to make this volume valuable as a textbook for medical students.

The authors have been assisted by 28 collaborators, all of whom are outstanding in their particular field.

This excellent volume on laboratory technique has been brought up to date by the addition of all the important new tests. It excels particularly in the two sections devoted to bacteriological, mycological and parasitological methods and serological methods. These two sections comprise 372 of the 870 pages. There are 380 figures in black and white and 12 colored plates. Fifty pages of index make reference easy. As a laboratory guide and reference book, it should be available to every clinical pathologist and laboratory technician.

OPAL HEPLER

SINCE there is no preface or foreword to *Fractures* by George Perkins², it is difficult to estimate the scope of the author's purpose. This book is a comparatively small one of 381 pages with a brief and perhaps inadequate index. It is written in a crisp, staccato style, and is almost outline in form. The illustrations are for the most part stippled line drawings, giving an elementary appearance far too diagrammatic to be useful to the student, as they in no way depict the contiguous soft parts which so often play a leading role in the management of fractures.

In many instances there are incomplete pages and the work as a whole cannot be taken as a good example of the bookmaker's art. It is entirely possible that this is due to the conditions under which it was published in London, 1940.

This book cannot be recommended for either student or practitioner as a textbook on fractures. It is essentially a handbook and will answer in a cursory way most fracture problems. Reading the book is analogous to attending a concentrated refresher course in fractures, and, as such, it may prove a useful adjunct to libraries of practitioners who may not have the time or facilities to go more deeply into a given subject in this field.

J. K. STACK

THE book by Griffith and Mitchell, *The Diseases of Infants and Children* has been revised and published under the title, *Textbook of Pediatrics*³. The authors have condensed and attempted to simplify the book so as to be more valuable for student use. The revised book is a compilation of the knowledge of over 60 authorities in various fields. However, in order to retain uniformity throughout the book, the authors have written the entire work, holding closely to their plan of condensation and readability.

Under the section on growth and development it is good to note that a knowledge of normal variations is stressed. This is especially valuable in pediatrics, a field in which preventive medicine is predominantly practiced.

¹APPROVED LABORATORY TECHNIC. CLINICAL PATHOLOGICAL, BACTERIOLOGICAL, MYCOLOGICAL, PARASITOLOGICAL, SEROLOGICAL, BIOCHEMICAL AND HISTOLOGICAL. By John A. Kolmer M.S. M.D. Dr. P.H. Sc.D. LL.D. L.H.D. F.A.C.P. and Fred Boerner V.M.D. 3d ed. New York: D. Appleton Century Co. Inc. 1941.

²FRACTURES. By George Perkins M.C. M.Ch. (Oxon) F.R.C.S. London and New York: Oxford University Press, 1940.

³TEXTBOOK OF PEDIATRICS. By J. P. Crozer Griffith M.D. Ph.D. and A. Gracie Mitchell M.D. 3d ed. Philadelphia and London: W. B. Saunders Co. 1941.

THE SURGEON'S LIBRARY

REVIEWS OF NEW BOOKS

THE excellent comprehensive book *Radiologic Physics*¹ is an outgrowth from the authors' experience in teaching the radiation courses at the University of Pennsylvania. At first glance the text appears formidable, but a further study shows that the mathematical considerations have been reduced to a minimum and proceed from elementary considerations into the more advanced material. Basic and fundamental information in theoretical and applied electrical engineering and radiation physics is treated in a simple, clear and accurate manner. The book is divided into two parts. The first part consists of a discussion of the theory and practice of electrical engineering as applied to radiological apparatus. The second part deals with the theory and application of x-ray physics to x-ray diagnosis and therapy and to γ-ray therapy. To aid the reader in the mathematical consideration of the subjects have been added an appendix which consists of a discussion of elementary trigonometry and calculus. This book is carefully organized so that it leads the beginner with very little knowledge of mathematics or physics to a firm foundation in the fundamentals of radiologic physics. There has been a real need for a textbook covering these phases of radiology. This volume deserves wide distribution and represents the most thorough discussion of radiologic physics available. It will be of particular interest to radiologists, teachers and students of radiology, but should be of interest to any physician who is interested in the use of electromedical equipment.

EARL E. BARTZ.

AS supervising editor of the *Supplement of The Practitioner's Library of Medicine and Surgery*² Dr. George Blumer states "There is probably no subject in which change takes place more rapidly than it does in medicine. The publishers feel in presenting this supplement that it covers important new work and brings up to date the entire system."

The first chapter on psychosomatic medicine is followed by one on neutron rays and artificial radioactivity by the recent Nobel Prize winner, John Lawrence. Full sections on chemotherapy and the vitamins are discussed in relation to their various forms by well known authors. Equine encephalitis, tetanus, rickettsiosis, pneumonia and pneumonitis are discussed as well as less familiar diseases such as Bejel and Letterer-Siwe disease.

Some sections are weak, largely because the subject is weak. The sections on therapy are well dis-

cussed, serum therapy in pneumonia, the use of vitamin K, sex hormones, dental caries, surgical relief of pain, surgery of patent ductus arteriosus are a few examples. The timely sections on the drug treatment of mental states and the chemistry and treatment of hypoparathyroidism are sections especially well handled. Many young authors are selected because of their subject interest. On the whole, I think this supplement is very well done.

M. HERBERT BARTZ.

THE second edition of *The Management of Obstetric Difficulties*³ by Paul Titus has been enlarged by the addition of 75 new illustrations and 85 pages of text. The chapter on the causes and treatment of sterility is complete, well illustrated, and of much practical value. Sella and Gamble and other new medical gynecals are discussed in the treatment of sepsis.

Old and modern classifications of deformed pelvis are given, and the technique of x-ray pelvimetry by the methods of Thoms and Caldwell and May is described in detail. The practical viewpoint of the author is indicated by his recognition of the necessity of considering the size of the fetal head in the problem of the diagnosis of cephalopelvic disproportion. Apparently however he is not familiar with the usefulness and wide application of the simple method of measuring the pelvis with the head. The procedures recommended, with which there might be disagreement, are few and mostly unimportant. In such a practical book, however the danger of extraction of the breech before the cervix is dilated, following Braxton Hicks' version, should at least have been mentioned if not emphasized.

The text is well illustrated and includes a number of colored plates, one of which is an excellent picture of positive pregnancy test in rabbit.

This text is the kind of book to which a doctor can turn for good advice on any obstetrical problem. The author avoids the discussion of controversial points and, on the basis of a generally sound obstetrical doctrine, gives the methods he has selected to be used in each condition. The man in general practice will find the book of much practical use for reference in any obstetrical difficulty and a valuable addition to his library.

D. W. S. HAZEN.

THE popular book *Readings in Interpretation*⁴ by Holmes and Ruggles has long since established itself as an excellent textbook for undergraduate students. The fact that this is the sixth edition of this classic

STUDENT MANAGEMENT OF OBSTETRIC DIFFICULTIES. By Paul Titus, M.D., and M. Louis The C.V. Mosby Co. 1944.

OBSTETRIC INTERPRETATION. By George W. Holmes, M.D., and Howard E. Ruggles, M.D. 6th ed. Philadelphia: Lea Febiger, 1944.

¹RADIOLOGIC PHYSICS. By Charles Koryl, B. and Raymond, Jr., and Duffell O'Neill. With foreword by Eugene P. Funderburg, M.D. Springfield, Ill. and Baltimore, Md. Charles C. Thomas, 1943.

²THE PRACTITIONER'S LIBRARY OF MEDICINE AND SURGERY. Supplement. New York and London: D. Appleton Century Co. 1944.

Many of the changes and reorganization in this book were necessitated by recent and newer knowledge. For example the chapter on vitamins is briefly summarized and brought up to date. The chapter on endocrinology has been modernized. The discussion of the thymus gland is shortened and made more clear and concise. The same change has been made in the discussion of the adrenal gland. The section on treatment gives a brief but usable dissertation on the new drugs and their uses.

Several new chapters have been added. There is a section on pediatric institutions and organizations.

This chapter is short and may give the student and beginner an insight into hospital organization. If so, it has served its purpose.

Following the section on physical growth and development is a new chapter on mental and emotional development. This section correlates the mental and emotional development with the physical and environmental factors.

It can be said without reservation that the authors in this instance have far surpassed their former efforts in forming a "Textbook of Pediatrics."

L. MARTIN HARRIS

BOOKS RECEIVED

Books received are acknowledged in this department, and such acknowledgment must be regarded as sufficient return for the courtesy of the sender. Selections will be made for review in the interests of our readers and as space permits.

ABOUT OURSELVES: A SURVEY OF HUMAN NATURE FROM THE ZOOLOGICAL VIEWPOINT. By James G. Needham, Lancaster, Pennsylvania. The Jacques Cattell Press, 941.

EPILEPSY: TO GENERAL LOCALIZATION: A STUDY OF THE MECHANISM, TREATMENT AND PREVENTION OF EPILEPTIC SEIZURES. By Wilbur Penfield, Litt.B., M.D. (Johns Hopkins) D.Sc. (Oxon., Princeton) and Theodore C. Erickson, M.A., M.Sc. M.D. (Minnesota), Ph.D. (McGill) Springfield, Illinois, and Baltimore, Maryland. Charles C. Thomas, 941.

PHYSICAL MEDICINE: THE EMPLOYMENT OF PHYSICAL AGENTS FOR DIAGNOSIS, TO THERAPY. By Frank H. Kress, M.D. F.A.C.P. Philadelphia and London. W. B. Saunders Co. 941.

STENOSES IN DIAGNOSIS. By Jonathan Campbell Meakin, M.D. LL.D. Boston. Little, Brown and Co., 7041.

THE MICROBE'S CHALLENGE. By Frederick Epton, Ph.D. M.D. Lancaster Pennsylvania. The Jacques Cattell Press, 941.

THE MODERN TREATMENT OF SYPHILIS. By Joseph Earle Moore, M.D. ad ed. Springfield, Ill., and Baltimore, Md. Charles C. Thomas, 941.

PRECLAMPIC AND ECLAMPTIC TOXICITY OF PREGNANCY. By Lewis Dexter, A.B. M.D. and Sonia Weiss, A.B. M.D. Boston. Little, Brown and Co. 941.

THE AUTONOMIC NERVOUS SYSTEM; ANATOMY, PHYSIOLOGY AND SURGICAL APPLICATION. By James C. White, M.D. and Reginald H. Smithwick, M.D. ad ed. New York. The Macmillan Co. 941.

DISEASES OF WOMEN. By Harry Sturgeon Gross, M.D., F.A.C.S., and Robert James Crossen, A.B. M.D. 6th ed. St. Louis. The C. V. Mosby Co., 7041.

ROENTGEN DIAGNOSIS OF THE EXTREMITIES AND SPINE. By Albert B. Ferguson, M.D. ANNALS OF ROENTGENOLOGY Vol. 7 New York Paul B Hoeber, Inc. 941.

GYNECOLOGICAL AND FEMALE ENDOCRINOLOGY. By Emil Novak, A.B. M.D. D.Sc. (Hon. Dublin) F.A.C.S. Boston. Little, Brown & Co., 1941.

GYNECOLOGICAL OPERATIONS. By J. Lyle Cameron, M.D. F.R.C.S. (Eng.), F.A.C.S., M.R.C.O.G. London. Humphrey Milford (Oxford University Press) 941.

SURGICAL BACTERIAL ENDOCARDITIS. By Edmund Libman, M.D. and Charles K. Friedberg. London, New York and Toronto. Oxford University Press, 941.

WORKER'S COMPENSATION AND THE PHYSICIAN: A MANUAL FOR THE USE OF GENERAL PRACTITIONERS TO IDENTIFY CARRIERS. By Henry H. Jordan, M.D. London, New York. Oxford University Press, 941.

PHRENOLOGICAL ANATOMY; FROM THE PHRENOLOGIST'S VIEWPOINT. By R. V. Gorch, A.B., M.D. New York. The Telford Co. 941.

BLOOD DISORDERS IN CHILDREN. By I. Newton Engelmann, M.D. Ph.D., Sc.D. Spitz. London, New York and Toronto. Oxford University Press, 941.

A HANDBOOK OF MIDWINTER; FOR PEDIATRICIANS, MIDWINTER, AND OUTSTANDING DOCTORS. By St. George Berkeley M.A. M.C. M.D., Cantab. F.R.C.P. Lond., F.R.C.S. Eng. M.M.S.A. (Hon.), F.R.C.O.G. 1st ed. London, Toronto, Melbourne and Sydney. Crowl & Co. Ltd., 1941.

SYMPTOMS OF GYNOSTRATRY DEVIANCE. By Austin I. Dodson, M.D. F.A.C.S. 3rd ed. St. Louis. The C. V. Mosby Co. 941.

THE TOXEMIAS OF PREGNANCY. By William J. Dickson, M.D. St. Louis. The C. V. Mosby Co. 1941.

SURGICAL PRACTICE OF THE LARRY CLINIC, BOSTON, MASSACHUSETTS. Philadelphia and London. W. B. Saunders Co., 941.

DIAGNOSTIC ROENTGENOLOGY. Edited by Ross Golden. 941 Renewal Pages. Vols. I and II. New York and Edinburgh. Thomas Nelson and Sons, 941.

OUR SEX LIFE: A GUIDE AND COUNSELLOR FOR EVERYONE. By Fritz Kahn, M.D. 3rd rev. ed. New York: Alfred A. Knopf, 941.

THE 1941 YEAR BOOK OF PATHOLOGY AND IMMUNOLOGY. Pathology edited by Howard T. Kainer M.D., Immunology edited by Sanford R. Hooker M.D. M.D. Chicago. The Year Book Publishers, Inc., 941.

SURGERY OF MODERN WARFARE. Edited by Hamilton Bailey F.R.C.S. Vol. 1. Baltimore: The Williams and Wilkins Co. 941.

THE 1941 YEAR BOOK OF INDUSTRIAL AND OCCUPATIONAL SURGERY. Edited by Charles F. Palmer M.D. Chicago. The Year Book Publishers, Inc., 941.

ENDOCRINAL ABNORMALITIES. By Noel A. Gillespie, D.M., B.Ch. M.A. (Oxon.), D.A. (R.C.S. Eng.) Madison, Wisconsin. The University of Wisconsin Press, 941.

THE DOCTORS MAYO. By Helen Chappell. Minneapolis. The University of Minnesota Press, 941.

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AMERICAN SURGERY IN A CHANGING WORLD

EVARTS A GRAHAM, M D, F A C S, St Louis, Missouri

IN the slow, painful progress of human culture and advancement there have been frequent interludes in which this movement has been stopped temporarily by the catastrophe of war. For a thousand years, however, no threat of an extinction of culture and of the finer qualities of our civilization has arisen equal to that which exists now in the appalling possibility of a victory of Hitler and of his Nazi barbarians. It seems fitting, therefore, that at the meeting this year of this great body of surgeons we should consider soberly some of the consequences upon our profession which the war may have, particularly in order that by thinking of them now we may perhaps be better prepared to prevent their occurrence.

It is almost incredible that the Germany of only fifty years ago in which there originated much of the groundwork of modern science, including many of the important developments of surgery, should have degenerated into its present position of practical denial of the true values of intellectual enterprise.

The Nazi philosophy of the supremacy of brute force can hardly be reconciled with the fundamental ethical principle of attempting to help the weak and the underprivileged patient which has always been the basis, and, may I say the glory, of medical practice at least

during the Christian era. Shirer,¹ in his *Berlin Diary* states that on May 6, 1940, Bernhard Rust, Nazi minister of education, said in a radio broadcast, "God created the world as a place for work and battle. Whoever doesn't understand the laws of life's battles will be counted out, as in the boxing ring. All the good things on this earth are trophy cups. The strong win them. The weak lose them." This authoritative statement from the man in charge of education in the Germany of today and possibly of continental Europe tomorrow, if taken at its face value, can mean only that in his opinion the purpose of education is to enable the strong to become stronger in order better to rob the weak. Surely that cannot be, some will say. It is unthinkable that anyone in a responsible position of authority could subscribe to so bestial a philosophy. But is not a sufficient answer to that complacent doubt to be found in what has already happened in the countries reduced to slavery—Poland, Czechoslovakia, Denmark, France, Norway?

Let anyone picture to himself the consequences if this conception of the ideals of education should dominate the world. In medicine no more humanitarian principles! Gone the charity hospitals! No more bother about crippled children! It is their own misfortune if the poor are sick and the children are crippled.

¹ Presidential address of the retiring president presented before the Clinical Congress of the American College of Surgeons Boston November 3-7 1941.

¹ Shirer, William L. *Berlin Diary* p. 328. New York: Alfred A. Knopf.

They are the weaklings. They 'will be counted out, as in the boxing ring. What of the effect of the glorification of such brutality upon the doctor himself and especially upon the surgeon? Is such a philosophy compatible with the kind of surgical practice with which you and I are familiar? Certainly not. Why carry out all the troublesome details to make an operation as safe as possible? If the patient is strong he will recover anyway and why worry if the weak does not survive? Doubtless the extreme results on the practice of surgery which I have just mentioned would not occur quickly but in the long run the corroding influence of a philosophy of brute force accepted by the dominant people of the European continent would be bound to degrade the present high standards which have been set up.

If then at the conclusion of this war Nazi influence should dominate the world a recurrence of the Dark Ages would seem to be inevitable so far as education and the progress of science is concerned. The spirit of the Spanish Inquisition would rear its ugly head again. Has it not already done so in those regions which have come under Hitler's control? The atmosphere of freedom necessary for the growth of science and the spread of education would not exist. German surgery since Hitler came to power has been practically sterile.

Those in America who because of the wide expanse of the Atlantic Ocean feel secure against the possibility of a successful Nazi military invasion may think that it is of little concern to us here whether or not Europe adopts the Nazi ideology. But I cannot agree with that opinion. It is admitted probably by everybody that if Hitler is victorious in the European conflict it will be necessary for the United States to remain on a war footing indefinitely. This will mean not only a large army and navy but large taxes also. We have become accustomed to depend on private benefactions for much of the support of our universities and hospitals. It is common knowledge, frequently expressed, that already the reduction of private contributions has seriously handicapped many of our institutions. If those contributions become still less because of higher and higher taxes for the support of a huge preparedness program, radical changes

in the whole scheme of higher education and of the support of scientific research will probably be necessary. It seems hardly possible that either education or research would be supported on the same generous scale if that support were dependent largely on government grants. Certainly much of the freedom to which we have long been accustomed in the privately supported institution would be curtailed with all the restraints, delays, and red tape necessitated by dealing with government clerks.

More important though might be the spread of the demoralizing Nazi theories of education to this side of the Atlantic which might be accepted under the impulse of necessity in competition even if they were considered undesirable. As long as three years ago reports from Germany indicated that the medical course had been shortened by a year and a half because of the demand for more medical officers in the Army. Is it inconceivable that such pressure might be made in this country for a shorter and 'more practical' training if we are forced to stay indefinitely on a war basis? The close integration of the world which has been brought about by modern transportation and communication has made it difficult even for an educational system of one country to be uninfluenced by that of another strong and dominating nation.

That science knows no political boundaries is a common remark. An idea expressed in one country is elaborated in a second and built upon in a third to emerge as something practical and perhaps utilitarian. Great accomplishments are necessarily the products of many minds and hands. Surgical science in its development has been no exception to this rule. The evolution of modern surgery has been the work of all the enlightened peoples of the world, and the chief contributions to it have been made by those who have lived in atmospheres of the greatest intellectual freedom. If Europe continues to live in slavery and the rest of the world becomes an armed camp there will be little prospect of any notable advance in any of the sciences or cultural activities even on this side of the Atlantic.

At a time like this when international hatreds are strongly aroused it is well to recall some of the epoch-making contributions which

have served to create our modern surgery. Although it is difficult, if not impossible, to date the beginning of any great movement, to say who actually started it, it seems reasonable to state that the birth of the modern scientific spirit of surgery can be traced more definitely to the immortal Englishman, John Hunter, than to any other individual. Before his time, and for that matter during his life (1729-1793), there was no experimental approach to surgical problems and no accurate knowledge of the pathological conditions present. Surgical operations for the most part consisted of amputations, the opening of abscesses, and the removal of superficial tumors. Hunter, however, by his resort to the experimental method, his careful study of pathological specimens, his observations on comparative anatomy and embryology established a scientific basis without which the surgery of the present day could not have developed. While Hunter was inaugurating the new sciences of experimental pathology and experimental surgery in England the army surgeon in Germany, according to Garrison, was still being called *Feldscherer*, because it was his duty to shave the officers.

To Great Britain, of course, also must go the credit of creating the antiseptic principle in surgery, carried to a revolutionary success by Lister, but later modified by the German, on Bergmann, into the technique of the present day asepsis. Lister's discovery, as everyone knows, made it possible for the first time to perform an operation on a patient without the previous fear of wound infection. The tremendous practical value of that work is likely to overshadow its other aspects. To me, however, some of those other aspects are of the greatest importance. Lister was a man of the same mental stripe as John Hunter. He was both a logical thinker and an experimentalist. From experiments which ran over a period of about twelve years he reached certain tantalizing conclusions about the nature of wound infection but he was unable to go further on his own knowledge. For example he had concluded that (1) putrefaction caused suppuration, and wound infection caused suppuration, and wound infection caused (2) suppuration, and wound infection caused (3) the gases in the air (the composition) was in some manner caused by the presence of air, (3) the gases in the air

were not responsible. What could it be in the air that was responsible, if not the gases? In 1865 his colleague at the University of Glasgow, Dr. Thomas Anderson, the professor of chemistry, called his attention to the papers of Pasteur on fermentation and putrefaction. Now he found the answer to his question. This to my mind is a splendid example not only of the interdependence of one nation upon another in science but of the interdependence of one science upon another. Was it not a revolutionary idea in itself at the time that a surgeon could receive help from a chemist on a "practical" problem like the healing of a wound?

Another major British contribution to the development of modern surgery has been the part played by the trained nurse. It seems doubtful to me that the art of surgery could have reached its present high plane without the sympathetic devotion to the patient and the careful attention to details which can be given only by intelligent women. The fact that Florence Nightingale and Joseph Lister were contemporaries has been of the greatest importance to us.

Germany through the influence of its great universities on medicine during especially the latter half of the nineteenth century and in the present century until the World War did much to extend the development of the scientific spirit in surgery. The older members of this audience will recall how eagerly the German surgical journals were read before the World War to learn of the latest developments in both the art and science of our profession and with what authority we at least in this country considered the German masters to speak. In looking back now, however, to the period nearly thirty years ago when German surgery was at its peak it would seem that what inspired us and fascinated us most was the spirit of scientific inquiry which was developed in that country to a greater degree than in any other up to that time. The best German university surgical clinics were centers of experimental investigation and were influenced by, at the same time as they themselves were influencing, other medical sciences, notably physiology and pathology. With the advent of antiseptic and aseptic surgery the German and

Our own surgery more closely resembles that of the British than any other. The differences are somewhat intangible and difficult to describe yet they are apparent. They can perhaps best be summarized by stating that we are more theoretical and less practically minded. We are a younger nation and, therefore, less conservative. The British surgeon is a master clinician in the application of the older art of physical examination to diagnosis and he is unexcelled in technical operative skill. He has carried on splendidly the tradition of anatomy as the foundation stone of surgery. We Americans, on the other hand, as a result of the changes in our undergraduate medical curriculum, have almost forsaken the gods of our fathers, anatomy and pathology. We have been seduced by the newer and more alluring gods of physiology and biochemistry. We have become more interested in function than in structure. It has been an amazing revelation to the American Board of Surgery to find that a generation of young surgeons has grown up whose ignorance of the anatomy and of the pathology of the structures with which they are dealing is abysmal. The wonder is that such men can be doing as good surgery as they undoubtedly are doing. Although the revelation shakes one's faith somewhat in the necessity of a sound knowledge of anatomy and pathology nevertheless, it is difficult to believe that these same men would not be doing much better surgery if they did have sounder knowledge of those subjects.

It is probably an inevitable characteristic of a young rapidly developing nation to become ambitious to equal or to excel the accomplishments of older nations. The spirit of inquiry and of experimental research prevalent in the better German clinics before the First World War found favorable soil on this continent when it was transplanted here by many young men who saw in the rapidly developing sciences of physiology and chemistry many applications to clinical problems. It is not surprising therefore that the stream of publications appearing in the German journals had a profound influence on American surgeons. Moreover this influence came at a time when we in this country were most able to take advantage of it. From the beginning of

this century on, more and more opportunities were presented to young men to undertake original experimental work. After the great awakening and the revolution in medical education which followed the publication of the Flexner report in 1910, together with the work of the Council on Medical Education of the American Medical Association, these opportunities were greatly multiplied. Experimental investigation and the spirit of scientific inquiry became glorified. The older more drab and less fertile disciplines of anatomy and pathology became seemingly of less importance to the ambitious young surgeon. His desire was to startle the world with a new and important discovery. Not much chance of doing that in the intensively cultivated and exhausted soils of anatomy and pathology. The urge to get into print to make his name known obsessed every young surgeon who was ambitious to get along. Positions of prestige and influence were often filled on a basis of the candidate's publications more than on any other qualification. Sometimes the list would be regarded as more imposing if the number of the published articles exceeded those of the rival candidate, without a sufficient regard for their quality. Is it any wonder then that this urge for recognition resulted in a dimming of the lights of anatomy, pathology, and the old established methods of physical examination of the patient?

One of the American characteristics most frequently noted by foreigners is our tendency to undertake a new project or to accept a new idea with the utmost vigor and enthusiasm. Our acceptance of the value of the spirit of research in medicine was no exception. The movement in this country developed into a veritable surge, and large numbers of young men crowded into the research laboratories to find out something new. The printing press was overworked to publish the volumes of work produced and scores of new medical journals appeared. There was little excuse for any Milton to be mute and inglorious. It was to be expected that most of the ambitious young investigators would be unfitted by nature to startle the world with any epoch-making discovery. On the other hand some, yes even some of the young surgeons, have

made very important fundamental contributions to our knowledge not only of physiology, both normal and abnormal, but even of pathology and of the forsaken subject anatomy, especially the anatomy of the nervous system. Others have added smaller stones to the building of our edifice. The spirit of research overflowed from this country into neighboring countries and back to Europe. With the benefactions of the Rockefeller Foundation distributed throughout the world there was scarcely a civilized country in which the spark of original investigation was not kindled into flame if it existed at all. Never before in the history of the world has there been anything remotely approaching the flood of scientific discoveries which has occurred in the last twenty years. Perhaps there will never be another period like it. In any case there is bound to be a recession of the wave. Almost certainly this recession has already begun. In all those parts of the world touched by the withering hand of Nazism research activities are impossible. England and Russia are handicapped by their struggle for existence. Only the nations of North and South America are so far free to carry on the spirit of research, and one wonders how long can this go on. Historians often have pointed out the wave-like character of the great cultural advances. During a relatively short period of time enormous progress is made, to be followed by a long period of relative inactivity or actual recession. Notable examples are the so-called Age of Pericles, the Alexandrian Period, and the Elizabethan Era. In view of the present chaotic conditions of the world, it would seem to require much optimism to assume that the period of unprecedented scientific advance through which we have just passed will continue with undiminished tempo.

Along with the recent period of enormous research activity there has been an immense improvement in the quality not only of the best but also of the average surgery practiced in this country. Better medical schools, more and better facilities for a long term specialized education of the young surgeon, more widely distributed well equipped hospitals have all had an incalculable effect in making good surgery available for the mass of the popula-

tion. The high standards set for certification by the specialty boards have been a very stimulating influence in keeping the practice of the various surgical specialties on a high level. The development of group practice brought to a remarkable state of efficiency by the Mayo Clinic and emulated by many other clinics has also been a factor in improving surgical practice.

The influence of the American College of Surgeons has carried much weight in improving the average surgical practice throughout the country. Its splendid work in improving the hospitals of the United States and Canada has already been mentioned. Also important have been its recently increased standards of admission to fellowship, the work of its recently appointed committee on graduate education, its official journal, and its annual meetings where the surgeon out of touch with the medical centers of the country can come to learn of the new developments in surgery.

At the meeting this year an innovation in the program was made. The Forum on Fundamental Surgical Problems was created. This symposium of ninety short presentations of experimental work on surgical problems was arranged largely by the efforts of Dr. Owen H. Wangenstein. It can almost certainly be said without fear of denial that never before at any surgical meeting in any country has there been a program presenting so much original work, mostly by younger investigators. It constitutes, therefore, a unique event. Moreover, it represents, it seems to me, one of the chief characteristics of modern American surgery, the spirit of inquiry and the utilization of all the sciences for the solution of surgical problems. It is a characteristic of which we American surgeons can justifiably be proud. It removes surgery from the realm of mere craftsmanship and translates it into a science. It is this experimental attack which constitutes the front line of surgery. Does not this program show that the spirit of the immortal John Hunter still survives? His memorable words to Jenner should be recalled, "I think your solution is just, but why think? Why not try the experiment?"

In the foregoing remarks an attempt has been made to emphasize the fact that the de-

velopment of modern surgery has been due to important contributions from several nations but yet that the practice of surgery has certain national characteristics which make it different in different countries. Reasons have been advanced for assuming that the recent unprecedented period of scientific progress is certain to be checked if it has not already been, regardless of the outcome of the war. A Nazi victory however will mean almost certainly for a time a more or less complete destruction of the scientific spirit throughout the world. It has been emphasized that attempts to preserve our present high standards and to carry forward the light of progress will fall most heavily on those of us who live in the Americas, South as well as North.

Let us now briefly consider some of the ways by which these standards can be preserved. I should say that it is of the utmost importance that the surgeons of North America and of Latin America come to know each other better and to develop a spirit of more sympathetic mutual understanding. The surgery that is being practiced in the centers of Latin America is not excelled anywhere and an increasing volume of original work of very high order is being produced. The knowledge of this work has been only slowly diffused in North America because of difficulties in language. Like wise for the same reason our surgery has not been so well known to our southern neighbors as the continental surgery. Would not a regularly meeting Pan American surgical congress with the cooperation of the American College of Surgeons provide a stimulating and helpful influence in preserving and fostering the spirit of surgical progress at least on this side of the Atlantic while Europe is recovering from the disaster of war? By meeting in different countries and at stated times, either annually or less often, there would certainly arise an inspiration from personal contact and from developing friendships and respects among those most actively engaged in the advance and practice of our profession. More of us North Americans would come to possess a knowledge of Spanish and Portuguese and more of the South Americans, English. There would be a freer interchange of medical literature of ideas and of students. The American College of

Surgeons already has a membership of 115 from Latin America. It could well be more nearly representative of all the Americas, both in membership and in its governing bodies, so that truly it would be an all embracing American College of Surgeons, thoroughly international in its point of view and administration. This suggestion may seem too radical but we must be prepared to make radical moves if we wish to counteract the results of the swiftly moving tragedy in Europe.

In a discussion of the preservation of our highly developed modern surgery it is necessary to touch upon our duties and obligations to the armed forces of our country in a program of preparedness for war. The Army particularly and to a less extent the Navy need more medical officers. We must do all in our power to provide them during the acute emergency. In striving to preserve our programs of training young surgeons we must not hamper the agencies of our government whose defeat would mean the destruction of our national independence. On the other hand, the armed forces should not unnecessarily and ruthlessly interfere with our laboriously developed system of training. Enough of it must be safeguarded to prevent too great a receding from our present standards. I am pleased to say here to the credit of the wisdom of Surgeon General Magee of the Army and of Surgeon General McIntire of the Navy that every effort has been made to interfere as little as possible with the training programs. Possibly a plan may be worked out whereby the young medical officers, after a limited service can be released to finish their periods of training in the civilian hospitals.

Possibly greater dangers to the safety of our resident system will come from the governing bodies of our civilian hospitals when the specter of hard times looms at them. We must, however hold fast to the principle of the system even if some modifications become necessary. We must not forget that surgery is a science as well as an art and must constantly advance. Above all, to be true to our profession, we must remember that the practice of surgery is based on humanitarian principles. Come what may we shall not subscribe to the philosophy of the supremacy of brute force.

ADRENAL CORTICAL TUMORS

The Types of Nonhormonal and Hormonal Tumors

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IN 1936, a study of adrenal cortical tumors was presented by a New York group from the Presbyterian Hospital. At that time it was shown that these tumors could be diagnosed by perirenal air insufflation Attempts were also made to determine the hormones excreted in these cases It was shown, that in adult females, normal or high amounts of estrogens were excreted in some tumor cases At the same time Gallagher found that large amounts of androgens were present in the urine of 2 of the adult female cases but his report was not completed in time to be included in the published paper but was incorporated in the reprints Since then the adrenal gland has been studied by numerous investigators and there has been a clearer understanding of many of its physiological activities Coincidental with the advances in the knowledge of the function of the normal adrenal there has been much experimental and clinical investigation into its pathological status Because of the better understanding of the clinical status with reference to adrenal cortical tumors, we believe that the report of a study of the adrenal cortical tumors which have been seen at the Squier Clinic is worthy of presentation

THE ADRENAL

The mammalian adrenal is actually two glands fused together in development Each has an essentially different origin, a different type of tissue and with a separate function, but they happen to be enclosed in one enveloping capsule and tissue stroma Tumors of the adrenal are not frequent When they arise they can be basically classified as follows

1 Tumors derived from the various layers of connective tissue, blood vessels, lymphatics, or nerve structures within the gland which are similar to such types of tumors that may occur in any other gland and as such are not peculiar to the adrenal They occur very rarely in the adrenal Tumors of these tissues having been reported as occurring in the adrenal are the following fibroma, lipoma, neuroma, neurofibroma, myoma, osteoma, hemangioma, sarcoma, lymphangioma, and melanoma

2 Tumors derived from the medulla are ones peculiar to that tissue and are of the ectodermal sympathetic nerve system They may be of the basic nerve cell, a sympathetic ganglion or secondly from the sympathetic the pheochromocytes or paragangliomas The first two occur more frequently in children and are seen more often than the latter, which occurring mostly in adults are rare

3 Tumors originating from the adrenal cortex are mesodermal glandular tumors, and cytologically are hyperplasias, adenomas, and carcinomas Accessory adrenals occur, called Marchand's bodies These are of cortical tissue and have been described as in the kidney, the perirenal fascia, the retroperitoneal fascia, within the broad ligament, attached to the ovary, or associated with the gonadal testicular tissues Tumors of these aberrant adrenals have been reported, all of cortical tumor type and, without and with, similar syndromes as are seen with adrenal cortical tumors Their occurrence is very rare

THE ADRENAL CORTEX

In a consideration of tumors of the adrenal cortex, it is essential to evaluate the more recent studies upon its embryology and briefly to review the marked advances of the knowledge concerning its biological processes

EMBRYOLOGY AND HISTOLOGY

The adrenal cortex originates from the mesoderm of the celom epithelium near the genital ridge and because of its proximity to that ridge Grollman has suggested that cells of the latter may be included with the adrenal and that hyperfunction of these cells may be responsible for the phases of reproductive symptomatology in those cases. The cortex during postnatal life gradually forms into three microscopic layers that are completed to the adult cortex, at or about puberty. The development of the inner of these three layers just before puberty has been shown by Miller Deansley and Whitehead to have some connection with the development at that time of the sexual glands and organs, and because of this it was suggested as an "A Zone" of the adrenal. In this latter zone because of his theory of inclusions in the juxtamedullary layer of testicular cells or rests, Grollman preferred to recognize a fourth zone or special androgenic zone.

A better understanding of the development of the adrenal cortex has been furnished by the studies of Alton, Bogmolez, Goormaghtigh, Hoerr and Zwemer in that the adrenal cortex apparently continuously grows from without inward. New cells are formed from the spindle-shaped fibroblastic cells under the fibrous capsule, develop through the three layers from without in the zona glomerulosa, zona fasciculosa, and zona reticulosa and during this process elaborate, accumulate, and discharge lipid sterols and then degenerating are absorbed in the reticulosa near the medulla. The secretion is discharged into the capillaries by the mature cells before their degeneration and the process is constant with replacement by new cells.

Under certain phases of hyperactivity there appear larger number of cells undergoing degeneration than is normally seen. This may suggest the possible reason for the widening of the reticulate zone at puberty (Deansley and Miller) the special zone (Grollman) and the appearance of granules in the cells with fuchsinophilic staining affinities as reported by Broster and Vines.

In relation to the appearance of discrete fuchsinophilic granules found in certain adrenals

in females manifesting virilism as reported by Broster and Vines, and Simpson and Joll the recent report of Sudds is interesting. She found that granules are present in 24 per cent of adult male adrenals and 38 per cent of female adrenals. In females the percentage of glands with granules showed a steady increase with age. With the exception of 1 fetus, in no case under 24 years were they apparent. This report is an excellent investigation of a small number of such sections reported in our previous article (Cahill et al.) in which such granules were found in dogs, in adrenals of individuals without virilism and more marked in adrenal cortical tumors with virilism. Sudds concluded that age has some influence on the presence of these granules, but sex plays no part. By inference from Sudds' conclusions, the presence of the increase of these granules in excess may be due to the aging influence of virilism when it occurs, and not that the granules were direct hormones which logically should be the sterols produced by the adrenal cells.

THE PHYSIOLOGY OF THE ADRENAL CORTEX

The adrenal cortex has been definitely established as the elaborator of hormonal substances, some of which are necessary for life maintenance. The hormonal substances have been shown chemically to be steroid lipoids.

Up to 941 over 20 closely related steroid derivatives have been prepared from the normal adrenal cortex. The action of all of these is not fully known. Of the identified steroids is one with the property of male sex hormone (dehydroandrosterone) (Reichstein) a beta kosteroid that differs only in its chemical structure from the testicular male hormone (androsterone) an alpha kosteroid. There has also been identified as secreted by normal adrenals the female sex hormones, estrone (Beall) and progesterone (Beall and Reichstein). Thus normal adrenals have the power to produce both male and female sex hormones. The excretion in the urine of androgens is small in children reaches a normal in adult life and diminishes after 40. It is relatively small in females. Part of these androgens are considered to be derived from the adrenal. The excretion in the urine of estrogens also

occurs in small amounts in normal males, normal amount in normal females, and part of these estrogens are considered to be probably elaborated by the adrenals

Some of the other steroids elaborated by the adrenal cortex have effects on the salt and water metabolism, the permeability of the capillaries, in the regulation of the carbohydrate, fat and protein metabolism, the renal function, the capacity of muscle response, and the resistance to stress. The maintenance of life and health is probably due to a combination of the various activities of these steroids. Of the identified steroids, one, desoxycorticosterone, seems to be most effective in the regulation of salt and water metabolism, in capillary permeability, and in preservation of renal function but has no demonstrable effects upon the carbohydrate metabolism. The properties of others of these steroids are not as yet clarified so that much further investigation apparently is necessary.

From the multitude of experiments reported there are suggestions that the adrenal may be implicated in many other metabolic processes. It has been shown that there is a relationship between the adrenal cortex and the gonadal pituitary system and that hyperactivity of the ovary may partially replace adrenal function (Rogoff and Stewart, Emery and Schwabe). It is of interest to explain the presence in comparative large amounts of vitamin C in the adrenal cells as shown by Szent-Gyorgyi.

PATHOLOGICAL PHYSIOLOGY

Since the adrenal cortex is composed of hormonal secreting cells, there are periods of cell growth or degeneration in which these cells do not elaborate hormones. Hyperplasia of these cells or tumor of these cells will have large numbers of this stage of cell life present without increase of hormones delivered into the capillaries. Again hyperplasia or tumor of the cells in the various stages of elaborating and secreting the steroid hormones will have an abnormal number of these cells present and as a result the secretion into the capillaries of an excess of some or all of the various steroids. Such has been shown to be the result of hyperplasia or tumor in the adrenogenital syndrome in which the excess amount of male hormones

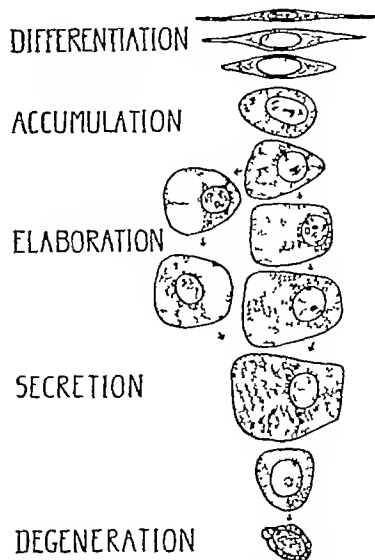


Fig 1 Diagram taken from Zwemer of the development of adrenal cells, showing the differentiation of the long cells from the cortex into the glomerular zone, the fasciculate zone and into the reticulate zone. During this process, they change, accumulate materials, elaborate substances, secrete them, degenerate, and are removed by macrophages and microphages near the medulla.

elaborated by the tumor has its effect upon the secondary sex organs. This has been shown to occur in the masculinization of females both children and adults and in the male maturity in male children (Simpson, Simpson, de Fremery, MacBeth, Gallagher, and Callow).

Hyperplasia or tumor cells at times have apparently elaborated excess amounts of steroids with female hormonal activity. The effect of these excess amounts of hormones may be registered upon the individual so affected. The feminism of a male has been shown to be the result of excess estrogens elaborated by a tumor of the adrenal cortex by Burrows et al, and by Simpson and Joll. There is then the suggestion that the presence of high amounts of estrogens as reported by Frank, from certain adrenal cortical tumors may naturally show no effect upon a female.

Bauer contends that an excess of the hormones which have the regulation of the electrolytes, salt and water metabolism, fat and sugar metabolism, are produced by the adrenal cortex either in the hyperplasia or in the tumors occurring in the syndrome described under many variations as Cushing's syn-

drome. This has been supported by the work of McQuarrie, Johnson and Ziegler and by Anderson and Haymaker.

It has been well established that the adrenals can elaborate androgens and estrogens as well as other metabolic hormonal steroids and there is suggestive evidence that the regulation of these secretions is subjected to if not regulated by stimuli from the pituitary. These androgens and estrogens can be present in excess quantities and responsible for symptoms present. They may result from some aberration of normal cortical steroid metabolism or they may be just an increase of normal production. Evidence is present that with some tumors there may be abnormal steroids produced. From such is the report of Butler and Marran of the steroid with male hormonal properties (pregnane 3-17-20 triol) associated with an adrenal tumor and they definitely established that such a hormone is not excreted by normal man or from a normal or pregnant woman.

In addition it has been shown by Butler and Marran and by Venning, Well and Browne that some patients with virilism and adrenal hyperfunction excreted pregnandiol and believed that this originated from the cells of the pathological adrenal.

CLINICAL CLASSIFICATION OF TUMORS

Up to 1928 it was relatively rare for patients to be seen in the Presbyterian Hospital who suggested adrenal pathology with the exception of the adrenal deficiency in Addison's disease. Since then because of increased knowledge and interest in endocrine diseases, hundreds of patients with symptoms of supposed adrenal disturbance have been admitted to the Squier Clinic. From the large number examined and the different investigations, the conclusion must be drawn that among adrenal syndromes the adrenal cortical tumor occurs infrequently. When it occurs it may be present without any evidence by symptoms that there is any change in the hormonal balance. In others it is accompanied by symptoms which are definitely due to hormonal influences. These symptoms vary according to the hormones secreted, their amount, and to the age and sex of the individual so afflicted.

The clinical groups, on the basis of proved cases may be classified as follows:

1. No recognizable hormonal changes
Changes due to excess androgens
 - a. In female child toward adult masculinity
 - b. In female adult toward masculinity
 - c. In male child toward adult masculinity
2. Changes due to excess estrogens
 - a. In adult male toward femininity
3. Changes due to excess androgens and other steroids
 - a. Cushing syndrome with associated sexual changes (mostly in females)
4. Changes due to excess other steroids related to metabolism
 - a. Cushing syndrome without sexual change (in male and female)

TUMORS WITH NO RECOGNIZABLE HORMONAL CHANGES

Tumors of the adrenal cortex have been reported in the literature as occurring without hormonal changes, (Hartung, Blacera, Stevens, Gibson, Loeb, etc.) They are infrequent and have been seen practically only in adults over 30 and have occurred in both sexes. When discovered they have apparently been present for a considerable period of time, first without any symptoms, but later with the complaint of pain in the side on which the tumor is present. Often when diagnosed the tumor was palpable. The deep situation of the adrenal and delay in invading any of the adjacent viscera for a considerable period before recognition allows growth of the tumor often to a large size. The pain is both abdominal and flank, and usually is made worse by exercise. Symptoms of malaise, fatigue and diminution of appetite are often present, especially in the larger tumors.

The following cases are illustrative of this type of tumor:

CASE A.B. Chart No. 6034, Presbyterian Hospital (reported in 1936) a single woman, aged 35 years, was admitted in 1927 complaining of intestinal trouble and pain in the left side for over a year. (It was occasional fever and weakness. She had missed her last menstrual period. She had a large mass in her left flank and cystoscopy showed that her left kidney was normal but was displaced downward by the mass. Her blood pressure was 55/65. There were no studies of urinary hormonal excretion. A transperitoneal operation removed a large tumor from above her left kidney. With the aid of a postoperative transfusion, she made an uneventful recovery. See

tions of the tumor showed a carcinoma of the cortex of the adrenal gland. In some areas there was a differentiation of the tumor with sections having arrangement of cells reminiscent in places of the different areas of the normal adrenal, the zona fasciculata, zona glomerulosa, and the zona reticularis. In other areas there was little or no such differentiation, but cells varying in size and shape and mitosis and infiltration. After 5 months' improvement there was recurrence of abdominal symptoms. While visiting in Nova Scotia she had an abdominal operation and a section of a liver metastasis was sent to us. This resembled the undifferentiated area of the original tumor. She was reported to have died 11 months after operation.

CASE 2 P J R., Chart No 16156, Presbyterian Hospital (reported in 1936), a male, aged 58 years, was admitted in 1915 complaining of shortness of breath for a year, progressive loss of weight and strength, and blood tinged sputum. His right pleura was aspirated and the fluid contained epithelial tumor cells. At autopsy there was found a tumor of his right adrenal cortex with metastases to pericardium, endocardium, lungs, liver, kidneys, and retroperitoneal tissues. He had no hypertension, no fat deposits, no plasma, hair or secondary sexual changes.

CASE 3 S S., Chart No 360795, Presbyterian Hospital, a male, aged 36 years, married and with children, was admitted in 1936 with pain in the left loin and chest for over a year. He had had a double herniotomy, an appendectomy, a tonsillectomy, and a cholecystectomy in the several years before admission. His left loin pain was in periods lasting 4 to 5 days. There was some loss of sexual vigor and with his pain he often had headaches and thought that these came roughly once a month. He was a vigorous male with a well marked normal hair distribution and with normal male genitalia. There was no hypertension. Cystoscopy and pyelograms were normal except that the inner border of the upper pole of the left kidney seemed shadowed by some tissue. A perirenal air insufflation showed a rounded tumor above and anterior to his left kidney. A large soft adrenal tumor, anterior to the anterior capsule of his left kidney was removed with the kidney through a flank incision. The adrenal tumor capsule broke at the time of removal. After an uneventful recovery he was treated with high voltage x-ray. Urinary hormones estimated immediately after removal of the tumor showed a low excretion of both androgens and estrogens (male 4 I U. and female 3 R U. per day).

Sections of the tumor showed that there was an upper small portion of normal adrenal that blended into the neoplastic. In the tumor part, there were collections of cells of unusual size containing enormous nuclei. The cytoplasm was pale, pink, and smooth. Multiple nuclei were present. Mitoses were occasionally seen. In places the tumor cells were much smaller and resembled the renal hypernephromas. Cells containing lipid vacuoles were not frequent. Areas of necrosis and hemorrhage were numerous.

Two years later the patient was readmitted with an abdominal mass which on transperitoneal exploration could not be removed because of its intimate attachment to the cava and aorta. Urinary hormones before operation showed male 15 international units and female 4 rat units, a low male excretion. High voltage x ray was resumed. He was readmitted 6 months subsequent to this with symptoms of general peritonitis. He refused operation, died, and on autopsy a perforation of a sigmoid diverticulum with generalized peritonitis was found. There was a metastatic tumor involving his aortic glands and his vena cava. Although the vena cava was involved, no metastases were found in his lungs.

CASE 4 A portion of a tumor of the adrenal was sent to us by Dr. M. W. Roome of the Department of Surgery, University of Chicago. This was from a male adult who had a large adrenal cortical tumor without any hormonal changes. The operative procedure was corroborated by autopsy. The cellular pathology of Dr. Roome's tumor was somewhat similar to that of Case 3, although the very large cells and nuclei were not as frequent nor did they appear as large lipid vacuolated cells were rare. Mitosis and infiltration were present.

CASE 5 A K., Chart No 652840, Presbyterian Hospital—Service of Dr. A. O. Whipple, a female, aged 50 years, single, was admitted September 1941 with loss of weight and strength for 8 months. Her history was negative except for menopause 12 years previously. Eight months before admission she began to have loss of appetite, weakness, and a gradual loss of 20 pounds. A mass then was seen to appear in her left upper abdomen without pain for the 4 months before admission. Because of a normal blood count and other tests it was thought to be a large spleen and was given x-ray treatments. With this and sunbaths she became darker in her skin. There was no increase in hair anywhere on her body, no changes in her breasts, and no headaches. She had no hypertension. From x-ray studies the mass was thought to be spleen. She was operated upon and a large tumor mass with dilated veins was removed. It was anterior and above the left kidney and was attached to but did not involve the kidney or the normal adrenal above. She made an uneventful recovery. Sections of the tumor showed cells resembling adrenal cells of the various types (similar to our Case 1). Cells with vacuoles were rare. The diagnosis was carcinoma of aberrant adrenal without hormonal symptoms.

Our 4 cases of adrenal cortical tumors, 2 males and 2 females, were all adults as was Dr. Roome's case. In each the tumor had been present for a considerable length of time and had reached a rather large size. Two presented symptoms of recurrent abdominal and flank pain on the side affected. All showed signs of malaise. One case was admitted in

growth of hair on face, and body all resembling the masculine distribution. Acne may occur on face or chest. The voice frequently becomes deeper and masculine in tone which has been explained as a lengthening of the vocal cords.

Changes occur in the secondary sex organs, but this change is a slower one than that seen in the menses and the hair. The younger the individual the more pronounced are the secondary sex changes. The usual sex organ changes are hypertrophy of the clitoris, deepening of the color of the labia, occasionally atrophy of the uterus and atrophy and loss of sensitivity of the ovaries. In young females the breasts may stay undeveloped resembling a boy at puberty. In older women atrophy may occur.

These changes have been shown to be associated with the appearance of excessive amounts of androgens in the urine. The amount of androgens excreted is proportionate to the masculinity changes that have occurred. The amount may be far above that excreted by males. From one of our cases Gallagher reported 480 international units per day and the average value for normal male in his estimation was 40 international units per day. The highest recorded figure has been in the case described by Slot in which the excretion was 2200 international units per liter. The male hormone isolated from the urine in some of these tumor cases has been identified as dehydroandrosterone.

Among our female adrenal tumor cases with hormonal syndromes, have been 2 in which the only apparent change was that which could be produced by excess androgens.

CASE 6. G. C., Chart No. 445624, Presbyterian Hospital, reported in 1936, aged 6 years, was admitted in 1935 complaining of hair upon the face and body, deep voice, and no menstruation. At the age of 13 she menstruated for 2 periods and then had complete cessation. Her hair became thicker and darker and grew on her face, arms, legs, and body. She sang bass and was troubled with acne. She had grown practically not at all since 13 years of age, but was very active and athletic. There was marked hypertrophy of the clitoris. The blood counts, chemistry, basal metabolic rate, glucose tolerance, and visual field determinations were normal. X-ray film showed fusion of 11 epiphyses. The left kidney was lower than the right and intravenous pyelograms

showed normal anatomical and functioning kidneys. Air insufflation roentgenograms revealed a small right adrenal and a large adrenal tumor mass above the left kidney. She excreted 1 her urine 8 rat units follicle hormones in 24 hours. Male hormonal excretion was estimated 480 international units in 4 hours. The left adrenal tumor was removed through an oblique subcostal transperitoneal approach. Her recovery was uneventful and rapid. Her menses returned in 8 days and have been normal for over 5 years. Her voice gradually registered higher. She has not grown since in height but her figure has become heavier and markedly feminine. The excess hair came off her body most markedly at menstruation, but her facial beard has persisted, but to a lesser degree. Air insufflation roentgenograms of the right adrenal taken a little over 1 month after the operation showed that that adrenal had hypertrophied. Estimation of her hormonal output 6 months after operation showed that both were in normal range.

Microscopic sections of the tumor showed areas of cells in loose strands arranged in masses and sheets, resembling in some places the reticulate zone and in others the glomerular zone but in most not resembling any particular area. No mitoses were seen but there was an apparent invasion of the capsule, and there were tumor cells in the blood vessels. A few areas of necrosis were present. There were also present numerous cells with vacuoles, which apparently consisted of lipoids.

CASE 7. R. R., Chart No. 57704, Presbyterian Hospital, aged 8 years was seen in 1939 complaining of hair on face and body and lack of menstruation. She had had normal menses from the age of up to 5 months before admission. She then missed a period, which was followed by a scanty period and there had been none since. At the same time hair appeared on her upper lip, chin, cheeks, chest and buttocks. Hair grew long upon her arms and legs and became darker. Her voice deepened. She had no pain or any other symptom. Her figure resembled a young male adult with male hair distribution. There was hypertrophy of the clitoris and slight hypertrophy of the labia. The pelvic organs were normal except for loss of usual ovarian sensitivity. There was no hypertension. The blood counts and the chemistry were normal. Basal metabolic rate, visual field and glucose tolerance tests were normal. X-ray films of skull, chest, and abdomen showed no abnormality. Air insufflation roentgenograms showed an ovoid tumor of the outer portion of the left adrenal. The right adrenal appeared normal. The excretion of male hormone in her urine was approximately 90 international units in 4 hours. During the same period she excreted 33 rat units of female sex hormones. At operation a ovoid tumor of the outer portion of the left adrenal was resected from the inner or normal portion through a left oblique transperitoneal approach. She made an uneventful recovery. Her menses returned to normal 1 month after operation.

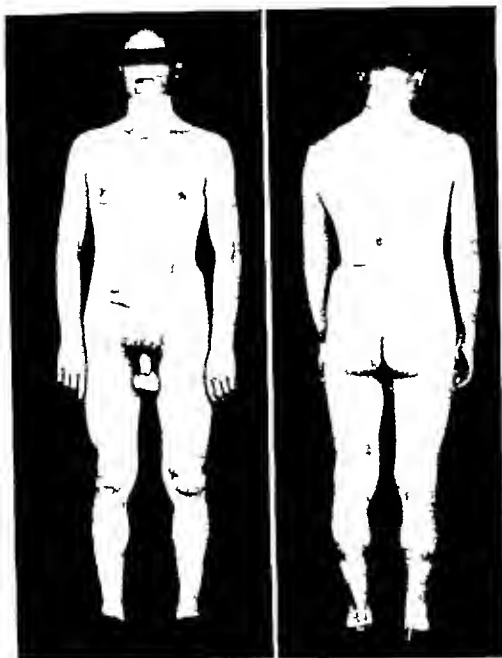


Fig 2

Fig 2 Case 3 SS, male, 36 years old, with left cortical adrenal tumor without hormonal changes

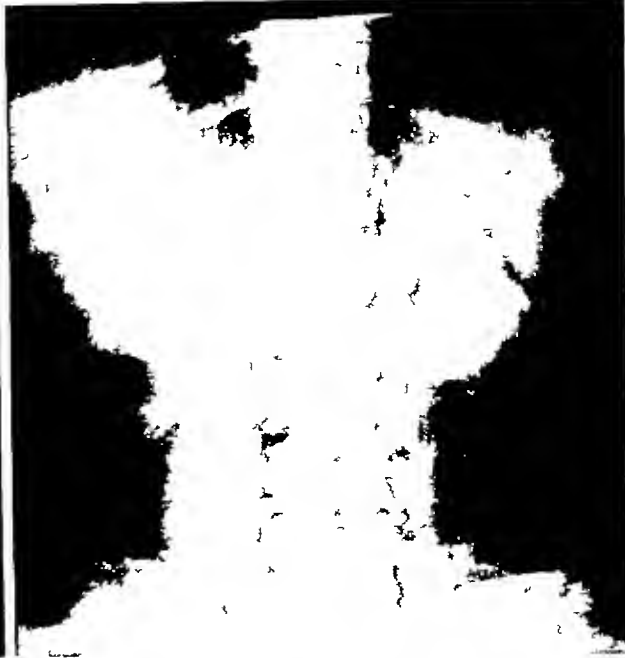


Fig 3

normal adrenal is visualized, near the side of the body of the 12th thoracic vertebral body

Fig 3 Case 3 Air insufflation x ray film of left adrenal tumor. The ovoid shadow superimposes upon the upper pole of the left kidney and the narrow compressed band of

Microscopic sections of the tumor removed showed a small area of normal adrenal tissue. The remainder was a tumor resembling in portions the glomerular area but mostly either without definite arrangement or in spots resembling the fasciculate and reticulate zones. The cells varied in shape, the nuclei were mostly round, the cytoplasm was granular, and at times sparse. There were no mitoses seen. Vacuolated cells probably containing lipoids were frequent.

Following her operation her breasts increased and the hair became less upon her body. Her voice became higher pitched. In the 6th, 12th, and 18th weeks following operation the excretion of hormones in her urine was 6 international units male hormone and 35 rat units female hormone in 24 hours.

She progressed without change in her menstruation but the hair remained upon her chin and neck. An insufflation air x ray film of her untouched right adrenal, taken in 1940, showed that the lower end had become rounded and wider. In March, 1941, she noticed that her menses had become scantier and that her hair growth was somewhat more vigorous. She was readmitted to the hospital and insufflation air x-ray films were taken showing that the lower end of the right adrenal had become rounded and resembled a tumor. Her excretion of androgens in the urine had again increased above normal.

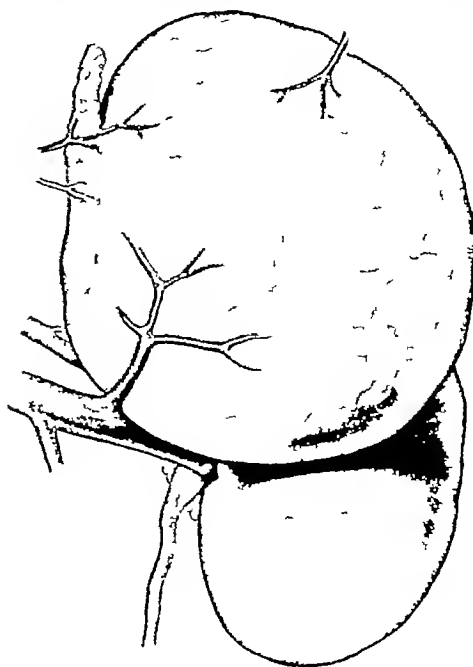


Fig 4 Drawing representing the tumor, the adrenal, and the kidney in Case 3

growth of hair on face, and body all resembling the masculine distribution. Acne may occur on face or chest. The voice frequently becomes deeper and masculine in tone which has been explained as a lengthening of the vocal cords.

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the excretion of excess androgens in the urine disappeared and there was a gradual diminution of the male characteristics and a restoration of the repressed female appearance and function

Changes in a male child toward adult masculinity The usual syndrome described with adrenal cortical tumor in a male child has been that of precocious puberty (pubertas praecox). In a very few cases tumors of the pineal gland have been responsible for sexual precocity in boys (Weinberger and Grant). Three cases have been reported as having been caused by tumors of the testis (Sacchi, Moreau, Parkes-Weber, and Rowland). A number of cases have been described in the literature without any proved cause. Among these has been a description of its familial tendency without tumor by Rush, Bilderback, Slocum, and Rogers under the term macrogenitosomia. The occurrence of the syndrome as caused by adrenal cortical tumor is uncommon. Kepler summarized its frequency as 12 times among 37 known adrenal tumors in children, a proportion of about 2 female children with pseudo-pubertas praecox to 1 male with pubertas praecox.



Fig 10 Case 7 Air insufflation x-ray films showing both adrenals. The ovoid mass above the left kidney clearly shows as an adrenal tumor.

Among the earlier cases was that reported by Linser in 1903, a boy of 5 with a left adrenal tumor with metastases. The second was by Adams in 1905. Player and Lissner re-

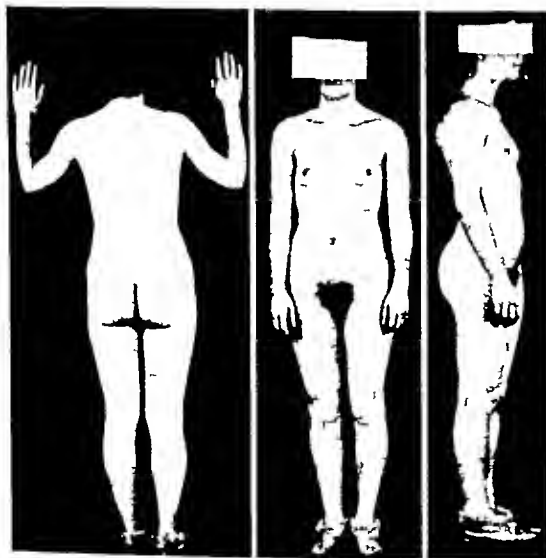


Fig 8

Fig 8 Case 7 R.R., 18 years, with a tumor of the left cortical adrenal with androgenic changes for 6 months. Her figure is male, her breasts flat. She has hirsuties.

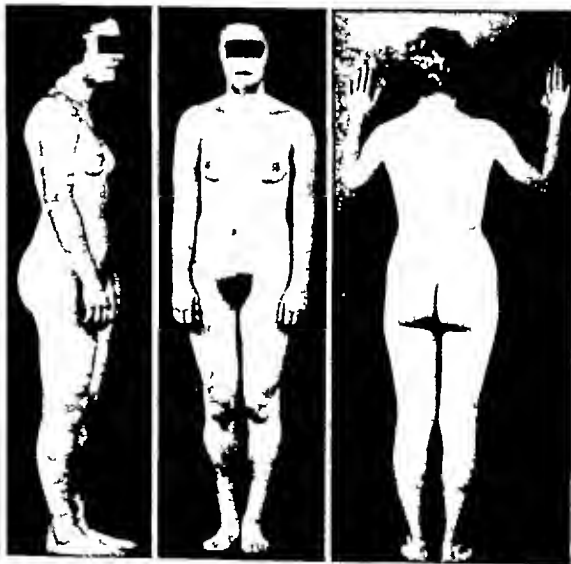


Fig 9

Fig 9 Case 7 R.R., 1 year after removal of a left adrenal tumor. Her figure and breasts are feminine but some hirsutism has persisted.



Fig 6 Air insufflation x-ray film of bilateral adrenal by periplasm in female 4 years of age with pseudosexual precocity. There was no tumor in this case.

She was again operated upon in April, 1941 and an ovoid tumor the size of a plum was resected off the lower pole of the right adrenal through lumbar incision. She made an uneventful recovery. Following the operation, she resumed her normal menstruation with the exception that they are accompanied by premenstrual pains, the first that she had had since the cessation of menses previous to the onset of the left adrenal syndrome.

Histological section of the right adrenal resembled that of the left. There were many cells containing lipid vacuoles.

These 2 cases presented tumors with secretion of marked excess of androgens. The androgens in both produced masculinization, less in the case with less hormones and marked in the case of excessive excretion. The diagnosis was confirmed in each by air insufflation x-ray films.

Removal of the tumors in each of these was not accompanied by acute adrenal deficiency because with only excess androgens secreted there was no reasonable expectation of function atrophy of the opposite adrenal. The uneventful recoveries support that reasoning. Following the removal of the tumors

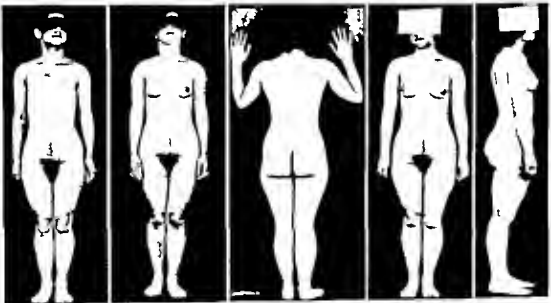


Fig 6.

Fig 6 Case 6. G.C. girl of 6 with tumor of the left adrenal with marked androgenic changes for 3 years. The left figure is before operation showing male torso and marked hirsuties. The right figure shows the change in month after tumor was removed. In this picture, the fig-

Fig 7.

ure is feminine; the breasts have hypertrophied and the hirsuties is less.

Fig 7 Case 6 G.C. 4 years after operation. The figure is still the same height, is decidedly feminine and has markedly less hirsuties.

the excretion of excess androgens in the urine disappeared and there was a gradual diminution of the male characteristics and a restoration of the repressed female appearance and function

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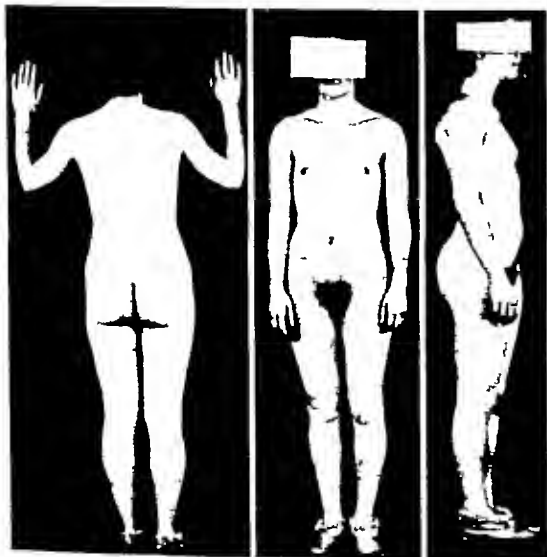


Fig 8

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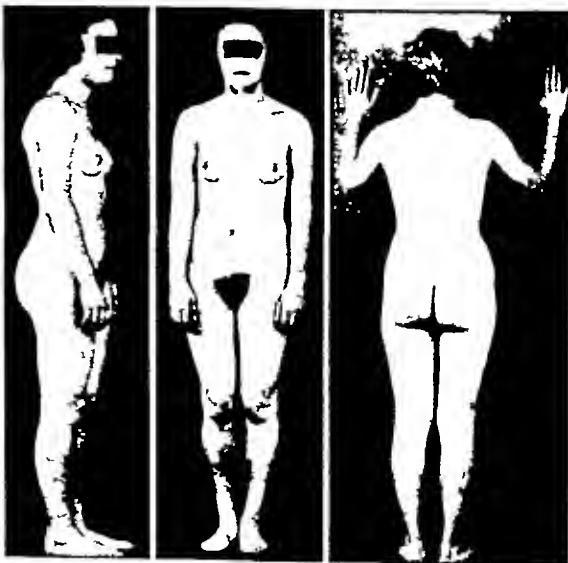


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Fig 9 Case 7 R.R., 1 year after removal of a left adrenal tumor. Her figure and breasts are feminine but some hirsutism has persisted.

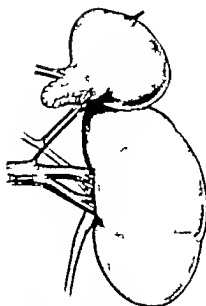


Fig. Case 7 Drawing showing the ovoid adrenal tumor growing from the outer portion of the adrenal, the inner portion as normal.

ported that up to 1933 only 8 authentic cases were found in the literature and they added theirs as the 9th. They also called attention to

2 cases reported in the literature by Laborde and by Marquand both of which had not been proved.

Cases of the syndromes must occur rarely without reporting either because of the marked advance of the disease before recognition, so that no operative procedure was undertaken and no autopsy was possible to prove the diagnosis. Broster in an exhaustive study of the subject recorded only 1 case of a male child with prematurity. Ian Fraser has recently published the occurrence of precocious puberty in a child of 1 year. From the few cases recorded the occurrence of pubertas praecox with adrenal tumor in male children is among the rarer adrenal tumors.

We have studied 5 male children with prematurity 5, 6, 8, 11 and 11 years of age. The 3 youngest presented masculine hair on genitalia, body beginning on the face associated with enlargement of the penis. In these 3 the testes were not proportionately enlarged. The 3 children were much larger than normal for their age and showed advance dentition and epiphyseal development. They had no adiposity or other metabolic change. Two showed no change in sella, no evidence of pineal enlargement, no change in the thymus and nor

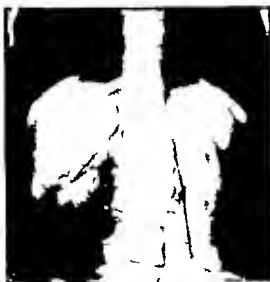


Fig. Case 7 Air insufflation ray film of her normal the time her left adrenal tumor was operated upon.



Fig. 3 Case 7 Air insufflation ray film year later showing the beginning of rounded tumor growth of the lower part of the right adrenal.

mal sized adrenals by air insufflation x-ray films One case, aged 6 years, showed a normal adrenal on the right and a large adrenal on the left by air insufflation x-ray film This was not confirmed because no operation was permitted and the case was removed from study after operation was suggested

Two boys, aged 11 years, showed marked hirsutism and hypertrophy of the genitals, including the testes Their symptoms had been present, one for 8 and the other for 7 years Their advancing maturity showed itself by fusion of all the epiphyses with apparent shortening of the extremities, and with their continued facial and muscular growth they resembled achondrodystrophic dwarfs but x-ray studies definitely disproved this dystrophy Both had prostatic secretion and sperm One of these boys showed no apparent change from normal in his adrenals by air insufflation x-ray films The other had an increase in size of his right adrenal No determination of its pathology was possible as no operative procedure was permitted These cases resembled closely the description of familial pubertas praecox reported by Rush et al

CASE 8 An additional case was observed by one of us (case of Dr O Pickhard) in a boy of 5 years in

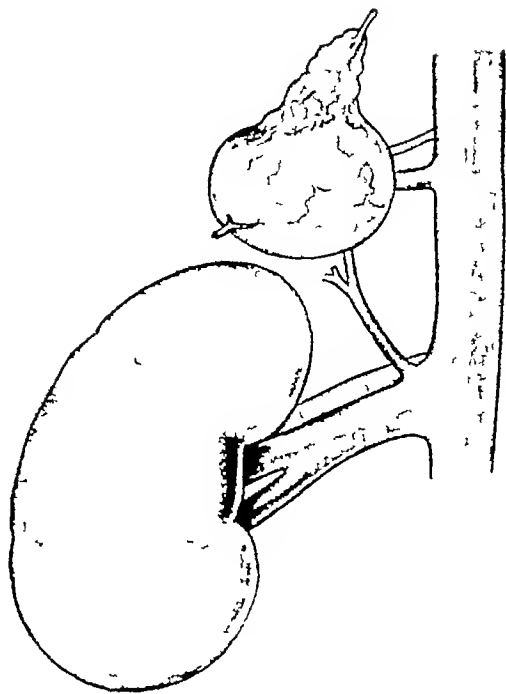


Fig 15 Case 7 Drawing showing the rounded tumor of the lower end of the right adrenal as disclosed at operation

the terminal stage of the syndrome This patient showed facial and neck obesity, as well as body obesity, genital hypertrophy, and a huge abdominal tumor



Fig 14 Case 7 Air insufflation x ray film 1½ years after operation, showing the increase in size of the rounded lower end of the right adrenal as compared with Figure 13

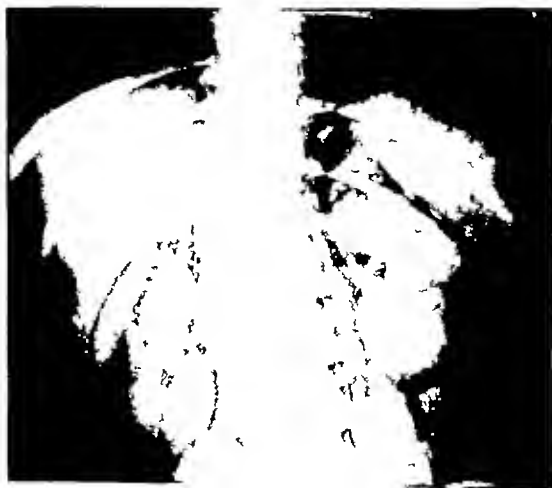


Fig 16 Air insufflation x ray film of a boy of 6 years with prematurity The right adrenal was normal, the left enlarged, whether hyperplasia or tumor not ascertained



Fig. 7 Case 9. Air insufflation x-ray film in male of 33, with some feminizing symptoms. The left adrenal is definitely enlarged and looks like a tumor on its inner side. \ operation permitted

Operative results on the few boys with the syndrome have had a very high mortality. In addition to the prematurity most obviously due to the effect of androgens, there appears very frequently symptoms suggestive of the changes seen with Cushing's syndrome and probably resulting functional atrophy of the opposing adrenal. In Fordyce and Evans case practically no adrenal tissue was found at autopsy on the opposite side. Mayer and Lissner a case the first surgical recovery in this group showed only the androgenic effect in his masculine maturity and in the acceleration of his epiphyseal growth. He showed no evidence of acute adrenal deficiency following the removal of his tumor and made an uneventful recovery.

TUMORS WITH EXCESS ESTROGENS

Only 6 definite cases of tumors with excess estrogens producing changes in the adult male toward femininity have been reported. The first was by Bittorf in 1919 a male of 26 years noticed decrease in the size of his testes and enlargement of his breasts. He became impotent and developed a tumor in the left side of his abdomen. Cachexia and death followed and autopsy (Matthias) showed a "malignant adrenal cortical hypernephroma." Zum Busch re-

ported a similar case with secretion from his breasts and the cause verified by autopsy. Holl reported a patient 15 years old who was operated upon the diagnosis established, but the tumor impossible to remove. He reported a second patient, 44 years old, with similar symptoms in which the tumor was removed by operation and recovery. Following recovery there was a subsidence of breasts, adiposity and varicoceles and a return of libido and sex function. Lissner published autopsy findings in a male of 33 years with breast enlargement and secretion and an adrenal cortical carcinoma. Simpson and Joll in 1938 published an exhaustive investigation into a patient, aged 34 years, who had feminization due to an adrenal carcinoma and excreted an excess of estrogenic hormone (probably estrone). The excess of hormone disappeared after the operation and returned with the recurrence of the tumor in the form of metastases. From the report of their case it is apparent that considerable proof is offered to explain the symptomatology of theirs and the previous cases.

Among the various cases referred to the Squier Clinic for adrenal determination was the following:

CASE 9. H.F. Chart \ 496469, Presbyterian Hospital, ged 33 years, as admitted in 1937 with a gynaecomastia of his stomach. He noticed that for 3 years before admission his hair had become finer than previously and was increasing over his body. He gained weight and his breasts began to increase and be noticeable. He noticed rather marked decrease in his penis and testes and a complete loss of desire and libido. He became easily fatigued and nervous. Areas of pigmentation developed upon his hands face and neck. His blood pressure low. He had a slight erythrocytosis, a normal sugar tolerance and normal blood chemistry. X-ray studies of his head and chest showed no particular abnormality. Perirenal air insufflation x-ray films showed large right adrenal and marked increase in the size of his left. Hormonal studies were not made due to his departure. There was no determined cause for his feminization but from observation upon hundreds of air insufflation studies of the adrenals he presented a shadow which showed a left adrenal many times the size of that normally seen and from its anatomical change suggested adrenal pathology.

From the few cases in the literature and especially from the one reported by Simpson and Joll, the adrenal in these cases was directly

responsible for the feminization, and the adrenal tumor cells were the source of the estrogenic hormone producing the symptoms. It was also shown by Simpson and Joll that androgens were still excreted by their patient. They attempted to show that histologically their case differed from an adrenal cortical tumor producing androgens, in one case of such with which they were familiar. Both tumors had numerous vacuolated cells, probably lipoids. They were unable to find fuchsin staining granules in the cells of the estrogenic tumor but they were present in the cells of the virilizing tumor. In the estrogenic tumor the cytoplasm of the cells were reported as diffusely fuchsinophilic. They suggested that from some studies on normal adrenals it appeared that granules were present in males in the inner layer of the cortex. In females they were not present except in patients over 50 years of age. Sudds in investigations on much larger number of adrenals, finding that granules are present in both sexes, concluded that they had little to do with sex and considerable to do with age.

Two of the reported patients with estrogenic tumors recovered from the operation when the tumor was removed and in neither was removal of the tumor followed by acute adrenal deficiency.

TUMORS WITH SYMPTOMS DUE TO EXCESS ANDROGENS AND OTHER HORMONES

From a study of the literature tumors with symptoms due to excess androgens and other hormones are not as infrequent as the others. In the large number of cases referred to us for determination of the adrenal status, this type appeared in many of the cases. A large number of the patients showed no apparent anatomical change in either adrenal. A considerable number had hypertrophy of one or both adrenals. A few had tumors as a causation. From the literature it probably is the most frequent type of tumor seen.

The syndrome was described by Cushing and he first suggested that it occurred with basophilic adenoma of the pituitary. The symptoms and clinical picture of his syndrome are characteristic of these types of adrenocortical tumors. Cushing outlined a clinical



Fig. 18. Case 10. Air-insufflation X-ray film in a woman of 36 years with a small right adrenal cortical tumor and a tiny left adrenal. Her symptoms were androgenic as well as of the Cushing's type.

picture consisting of a rapid, plethoric, painful obesity, affecting primarily the face, neck, and abdomen but usually sparing the limbs, thus giving rise to an obesity described as the "buffalo type." The facial changes made the eyes appear small and slit-like, resembling a pig's eye. There was acrocyanosis, with purplish linear atrophiae on the lower abdomen and the thighs. Hirsuties was marked. There was a tendency toward polycythemia and hypertension and glycosuria was of frequent occurrence, as were high blood cholesterol readings. With the syndrome was muscular weakness and porosis of the bones causing a cervicodorsal stoop and a shortening of the stature. Amenorrhea was present in the females and impotence in the males. There was a marked susceptibility to infectious processes and to physical stress. Mental changes were present, and in some, well developed psychoses occurred.

Since the description by Cushing, many reports have been issued as to the findings in these cases in which opinions have varied as to the causation. Some believe it mostly pituitary (Pardee). Others reported that it was more frequently associated with adrenal changes (Oppenheimer et al., Silver, etc.). Some similar syndromes have been reported



Fig. 9. Case. Air insufflation ray film in case of 40 years old boy with tumor of the right adrenal cortex. The air did not diffuse between the liver and the tumor because these fascial planes were sealed by adhesions.

as having been associated with thymic tumors. A few rare cases with obesity and hypertension as well as hirsuties have occurred with the arrhenoblastomas described by Robert Meyer.

From a study of the recorded cases with the probable causation factors as far as hormonal changes have been registered upon the patient some of the changes could most likely have been due to the effects of excess androgens. These changes were the hirsuties, amenorrhea and changes in the secondary sex organs as breasts and clitoris. Some of the cases exhibited these changes to a marked degree others less. The fat deposits, the skin the poly cythemia, the hypertension, and glycosuria as well as the weakness and osteoporosis can best be explained by excess hormones present, disorganizing such metabolic processes. Bauer called attention to the fact that these in their main effects were the opposite to Addison's disease and that most of these individuals were suffering from an excess of metabolism steroids produced by the adrenal either by itself or through stimulation of the pituitary. Considerable support to this has been offered by clinical observers and by investigators.

When tumor occurs the cases may vary from those with marked sex changes and milder Cushing type changes to those with less marked sex changes and mostly of the syndrome described by Cushing.

The following 3 cases show the variations.

CASE a. L.P. Chart No. 450260, Presbyterian Hospital, reported 936 married woman aged 36 years was admitted 1935 with loss of hair of her scalp excess of hair over her body and absence of menstruation for 3 years. She had become stouter and was very nervous and had attacks of palpitation. There was hypertrophy of her clitoris. She had mild erythrocytosis but her chemistry, basal metabolic rate, etc. were normal. X-ray films of skull, chest and abdomen showed no abnormality. Cystoscopy and pyelography were normal. Air insufflation ray films showed an ovoid tumor of the right adrenal and small left adrenal. She excreted 60 international units of male hormones in 24 hours. During her stay she was slightly depressed at times and emotionally unstable. Her right adrenal tumor was removed through oblique transperitoneal incision. She developed an acute adrenal deficiency, and in spite of saline, blood, and the then available cortical extracts she died following convulsion 3 hours after operation. Autopsy permitted.

The tumor on section was very cellular and not well encapsulated, and through most of the tumor were cells in sheets cords, and nests. The cells are large with pale vesicular nuclei and indistinct nuclei. There was an occasional mitosis and tumor cells were found in the adjacent tissue. There were areas of necrosis. The cytoplasm of the cell was abundant granular and many were so vacuolated as to be foamy.

CASE b. L.F., Chart No. 240269, Presbyterian Hospital, reported 936 female, aged 36 years, was admitted 1939 with headaches, weakness, palpitation, excessive growth of hair and cessation of menses for 3 1/2 years. She was married and had no children. Her face and hands were reddened, dark, and puffy and she had edema of shoulders and abdomen and striae of abdomen and thighs. There was marked loss of hair and best. There was an indistinct mass in the right flank, hypertrophy of the clitoris and insensitivity of the ovaries. She showed an erythrocytosis, normal blood chemistry, high basal metabolic rate, low sugar tolerance, and hypertension. She excreted 8 rat units follicular hormones in her urine in 24 hours. X-ray studies of skull and best showed no abnormalities. The right kidney was low but no abnormality by pyelogram. Air insufflation ray film showed large mass between the right kidney. The air did not diffuse between the liver and the mass. This mass an adrenal tumor was removed through transperitoneal approach. It was adherent to liver and vena cava. She developed an acute adrenal deficiency 24 hours but



Fig 20

Fig 20 Case 12 Air insufflation x ray film in a woman of 40 years with androgenic symptoms as well as Cushing's, showing a similar irregular mass above the right kidney resembling Case 11

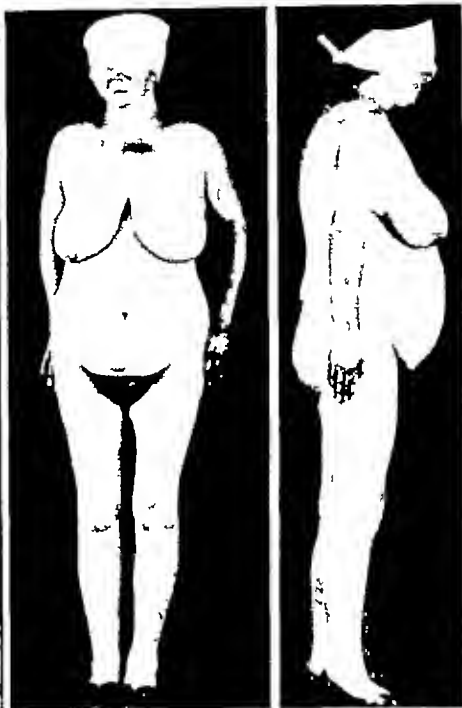


Fig 21

Fig 21 Photograph of Case 12, showing duskiness of hands and neck, cervicodorsal stoop, trunk and face obesity, and thinness of hands and legs, abdominal striae, and mild hirsuties

recovered with saline and blood transfusions. Her menses returned after 2 months and her hair diminished in amount. She returned to her marital status with return of libido. Six months later she developed headaches and her menses became scanty at first and then ceased. X-ray films showed lung metastases. The hair growth, duskiness of hands and feet, and edemas progressed. When she died no autopsy was permitted.

The tumor on section showed that the morphology was almost identical in all parts. There was no resemblance to a normal adrenal. There were many mitoses and cellular invasion of the stroma. Many cells were vacuolated and foamy cells were frequent.

CASE 12 E G, Chart No 304917, Presbyterian Hospital, a female, aged 40 years, was admitted in 1939 with complaints of hair on body, increased fatty deposits, and absence of menses. For several years her entire appearance had changed with gain of fat on face, neck, chest, and abdomen with loss of size of arms and legs. Her face, chest, and hands were reddened. She had marked striae on the abdomen and thighs. With this change her menses had ceased. She had dyspnea and edema of her feet. Her clitoris and labia were enlarged. She had erythrocytosis, a normal blood chemistry, a low basal metabolic rate, and low sugar tolerance and a high

blood cholesterol reading. There was moderate hypertension and a rather moderate cervical dorsal stoop. X-ray films of her skull, bones, and chest showed no abnormalities. Air insufflation of the perirenal space showed an apparent large mass above a low right kidney resembling that in Case 11. There was no follicular hormone in her urine and only a small amount of follicle stimulating hormone was present. Male hormonal excretion determination was not done. She was not operated upon but condition became worse and she returned to Poland. Since then she has been untraced.

These 3 cases appear to be illustrative of the variations produced by different effects. The first had well marked effects of excess androgens and moderate other metabolic disturbances and the last with slight change in sexual characteristics and well marked metabolic disturbances. These cases differed markedly from the 2 younger women in the emotional balance. In fact it seems as if the Cushing type tumor appears more frequently in the older group of women. The cases with only androgen syndromes were stolid, not nervous.

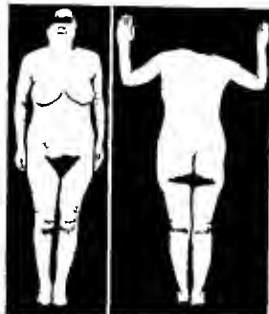


Fig. 2.

Fig. 2. Case 3. Photograph of female aged 27 years with syndrome of Cushing's type without androgenic changes. She had tumor of her left adrenal cortex.



Fig. 3.

Fig. 3. Case 3. Air infiltration x-ray film in which the air diffuses poorly above normal sized right adrenal and tumor of the left adrenal above her left kidney.

took all examinations without any disturbance. Those with the other changes were nervous, apprehensive, and difficult to handle. The demonstration of the tumor by air injection became less clearly defined as the patients developed fatty deposits and edema. In 1 case the second the air did not diffuse between the tumor and the liver or around the mesial aspect. Operation disclosed that tumor adhesion had sealed the fascial planes in this area. The last patient, not operated upon, presented a similar air infiltration x ray film. The first case was proved to have an excess of male sex hormones excreted in her urine. The second case most probably had a large excess but at that period there was no satisfactory process available for its estimation. She however excreted normal amounts of female hormones. The 3 patients operated upon developed postoperative symptoms of acute adrenal deficiency. One patient died in spite of therapy now known as inadequate. The other patient recovered from her acute deficiency. We thought at first the recovery was brought about by our therapeutic endeavors but later

experience leads us to think that the hormonal production of her unrecognized metastases may have played the major part in her recovery.

TUMORS WITH CHANGES DUE TO EXCESS OTHER STEROIDS RELATED TO METABOLISM

CASE 3. L.G. Chart N. 509497 Presbyterian Hospital, a female aged 27 years, was admitted 937th marked depression melancholia and with suspected endocrine pathology 1 1/2 years before admission she was normal married woman working journalist and editor. She then underwent marked change: personality lost interest in her surroundings, contact and body needs. At the same time her menses ceased and fine silky growth of hair appeared upon her face body and extremities. There was no resemblance of male distribution. There was swelling and dusky color of face and hands. Ringing of neck, shoulders and abdomen with trace on her abdomen. She had cervical thoracic stoop. She was apathetic and sat long periods without speaking or moving and walked latterly. She stated that she was mentally unbalanced. Her clitoris was small as were her pelvic organs. She had a erythrocytosis, normal blood hematuria with high cholesterol reads 400. A low sugar tolerance and a normal basal metabolic rate. There was mod-

crate hypertension. The x-ray films revealed no abnormalities of head, chest, or bones. Perirenal air insufflation x-ray films were difficult to read because of poor diffusion of the air. However, by serial readings a normal appearing right adrenal was identified and a triangular shaped tumor on the left was noted. There were no demonstrable male or female sex hormones in her urine by our ordinary comparative examinations. At operation a left adrenal tumor was removed through a subcostal transperitoneal incision. She reacted excellently from the anesthesia and on recovery from unconsciousness was talkative, and chatty, greeted her relatives the first time since the onset of her syndrome and stated that she no longer felt unbalanced. Her relatives declared she acted like her former self. She was given large amounts of saline and commercial cortical extract then available. In 20 hours she developed acute adrenal deficiency, was benefited slightly by transfusion and cortical extract but died after a convulsion in 23 hours after the operation.

A complete autopsy showed Cushing's syndrome (clinical) hirsutism (silly, not masculine) adiposity, adenoma of adrenal cortex, left, (surgically removed), atrophy of adrenal cortex, right, encephalomalacia, frontal, right, fatty liver, normal ovaries, thyroid and pineal. In the pituitary, all basophiles showed marked hyaline changes in their cytoplasm. Partial to complete disappearance of the granules, vacuolization and disfiguration of the nuclei (Crooke syndrome).

The left adrenal tumor showed a small group of cells alternating with much larger cells which had a foam cell appearance. The true adrenal cortical zones were not seen. The group of cells seen were large, polygonal, possessing oval nuclei with distinct nucleoli and were at times vacuolated. The foam cells appeared multinuclear with rather small nuclei and pale framework within the cytoplasm. A tendency to giant formation was rarely seen.

This patient had the symptoms described as Cushing's syndrome with cessation of menstruation, the only real change of sexual character. No male or female urinary hormones were identified by the usual examination. The complete autopsy did not reveal any change in the pituitary except that described by Crooke. It is to be deduced that the adrenal cortical tumor produced the changes manifested by her symptoms for the 2 years prior to her operation. The death was due to acute adrenal cortical deficiency. The remaining adrenal was apparently atrophic and inactive. In retrospect the tumor must have produced sterols in abundance as was evidenced by the histological sections in which most of the cells were foamy with lipoids. These sterols were

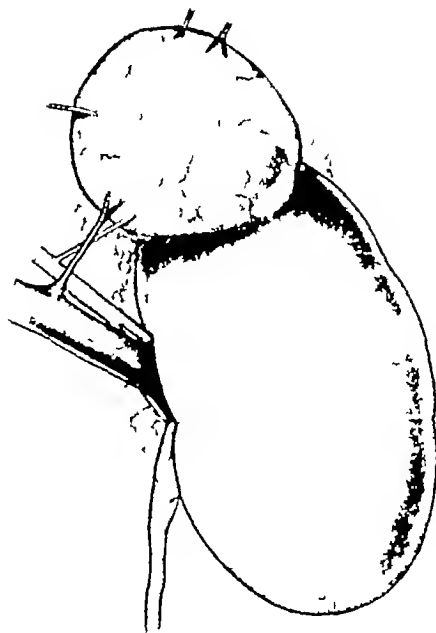


Fig. 24. Case 13. A drawing of the tumor and kidney at the time of operation.

neither of androgenic nor estrogenic influence as was shown by her symptoms and the failure to identify either in her urine. From her symptoms and acute death following the removal of the tumor they apparently had to do with the life maintenance properties of the adrenal.

DIAGNOSIS WITH AIR INSUFFLATION X-RAY FILMS

For the purpose of ascertaining the anatomical change in the adrenal gland we have used the x-ray studies of air insufflation into the perirenal fascial spaces. We have previously reported upon this technique, as have Roome, Mencher, and others. Normal adrenals are usually well visualized if sufficient air is introduced in the proper plane. The right adrenal more frequently shows as a long thin wedge between the liver and the psoas and the left as a less dense wider wedge or crescent above the left kidney. When tumor is present it is more clearly shown in thin people. The tumors are round when small, ovoid when larger, and may be lobulated when very large.

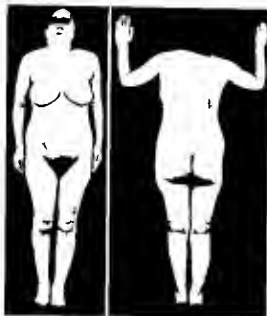


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experience leads us to think that the hormonal production of her unrecognized metastases may have played the major part in her recovery.

TUMORS WITH CHANGES DUE TO EXCESS OTHER STEROIDS RELATED TO METABOLISM

CASE 3. L.G. Chart N 509407 Presbyterian Hospital, female aged 27 years was admitted 1037 with marked depression, melancholia and with suspected endocrine pathology. Up to 3 years before admission she was normal married mother, working as journalist and editor. She then underwent marked change: personality lost all interest in her surroundings, contacts, and body needs. At the same time her menses ceased and fine silky growth of hair appeared upon her face, body and extremities. There was no resemblance of male distribution. There was swelling and duskliness of face and hands, swelling of neck, shoulders, and abdomen with tissue on her abdomen. She had cervical thoracic goop. She was apathetic and sat long periods without speaking or moving and walked listlessly. She stated that she was mentally unbalanced. Her clitoris was small as were her pelvic organs. She had erythrocytosis, a normal blood chemistry with high cholesterol reading. A low sugar tolerance and normal basal metabolic rate. There was mod-

Estrogens Frank early called attention to the excretion of large amounts of estrogens in the urine of patients with the adrenogenital syndrome and with virilism. In our former article we called attention to the large or normal amounts so excreted. Slot and Kepler each reported cases in which there was no excess. In the series of Levy, Simpson, de Fremery, and MacBeth, a slight excess of estrogenic hormone occasionally occurred. In our present reported cases we have shown that in young girls with virilism due to a tumor a high amount of estrogens was excreted before the tumor was removed and continued unchanged after removal of the tumor and the virilism had recessed.

Of particular necessity is the estimation of the estrogens in those rare cases of males with femininity due to adrenal cortical tumor. Here, Simpson and Joll have shown that excess estrogens were evidently present before the tumor was removed, disappeared after the tumor was removed, and recurred with reappearance of the tumor. The estrogen excreted was considered to be estrone.

The identification of other steroids associated with adrenal cortical tumors is as yet in an unknown state. An increase in substance which maintains life was demonstrated in the blood stream of a patient with hyperfunction of the adrenal cortex (Cushing's syndrome). The identification of like-maintaining substances in the urine in normal persons and their increase under stress has been reported by Weil and Browne. There are as yet no reports upon cases of adrenal syndromes in which these other types of steroids have been identified in the urine, or whether their amount can vary according to the adrenal symptoms.

OPERATIVE PROCEDURES

Three different routes of approach have been used for removal of the adrenals: (1) extraperitoneally, through the lumbar region, (2) transthoracic route, and (3) transperitoneal route.

The lumbar route with extraperitoneal approach has been used extensively in adrenal operations by Crile. It has been used for removal of tumors by many operators. Wal-

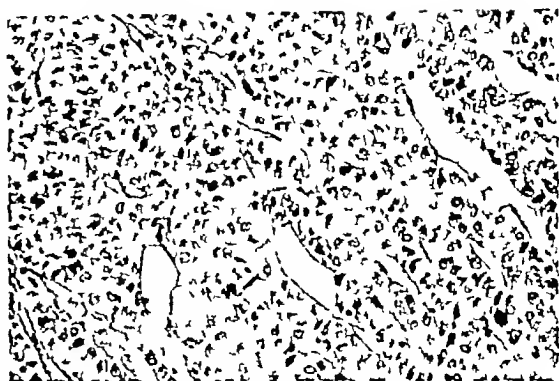


Fig. 26. Section removed in Case 5, a female without hormonal symptoms. The tumor was of an aberrant adrenal. Sheets of cells of somewhat uniform size arranged in places resembling the different zones of the adrenal. Lipoid vacuoles are rare. The adrenal tumor from the other female without hormonal symptoms had similar histology. $\times 160$.

ters, with as extensive experience as any, has used this route and has done bilateral exposures to determine first the diseased side and second to observe whether there was an opposing adrenal. Young devised an ingenious retractor fashioned after the rib-spreader retractor for chest operative procedures, and used the retractor for simultaneous bilateral exposure. The lumbar route has been used by us in adrenal operations upon the nontumor cases. It was used in 3 tumor cases: (1) a small pleochromocytoma of the adrenal, (2) a small tumor of the lower pole (Case 7), and (3) one of the larger nonhormonal tumors occurring in a male. This latter was difficult to deliver, was attached to the anterior capsule of the kidney, and the tumor ruptured through the capsule when attempts were made to visualize the tumor vessels before clamping and ligation. It was necessary to remove the kidney with the tumor.

The transthoracic approach was used by Broster in cases of nontumor adrenogenital syndromes. This, he claimed, was the easiest approach in view of the fact that the adrenal vessels allowed a slight range of upward movement. It has, however, the disadvantage of creating an artificial pneumothorax. It also was necessary to do a preliminary laparotomy for exploration of the adrenals by palpation, and then after recovery to perform the main operation by the transthoracic approach.

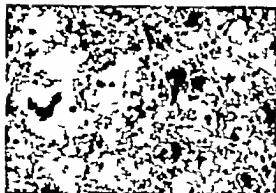


Fig. 5. Section removed in Case 2, male, without hormonal symptoms. The cells in places are gigantic with large amounts of cytoplasm and huge nuclei. Lipoid vacuoles are rare. All male cases without hormonal symptoms had similar histology. $\times 60$.

All of the tumors so diagnosed by us were confirmed by operation. In a number of cases in which no tumor was shown on the air insufflation x ray films, but with some hypertrophy apparently present, operative procedures have always demonstrated that the adrenal was exactly as outlined. It was especially valuable when tumor was present and small and unrecognizable by any other method, except operation. It will also show the presence of the opposite adrenal if one is the seat of a tumor. In children and in thin adults the air diffusion is easy and gives clear shadows. In obese and especially in those with Cushing's syndrome the air diffuses poorly because of the fatty edema in the perirenal tissues. In these patients a series of films may outline parts of the tumor so that a composite film may be made. For the purpose of demonstrating adrenal anatomy in our hands the use of air insufflation has been without complications and without fatalities. If used often it can lead to an increase in the fibrous tissue in the perirenal fat and by some this has been considered to be a hindrance during operation. Compared with the diagnostic aid obtained by its use in our hands, the increased fibrosis of the perirenal fascia was of no consequence.

The autographic x ray film by the method of Reynaldo dos Santos has been used by some but the dangers of thorotrast have been since shown to make this media hazardous.

HORMONES

Androgens. The earlier work of the estimation of the androgenic hormones was by the capon comb growth. The method is better standardized but difficult and expensive. The colorimetric method when used, as by Callow with proper caution as to procedure and interpretation, is simpler and less expensive and time may prove its value. There is definite agreement that virilism and adrenal cortical tumors are associated with high levels of androgen excretion and this high androgen excretion declines to lower levels after operation.

The determination of the particular hormone or hormones producing androgenic effect is a difficult procedure requiring high output values in the urine and large amounts for assay. The hormone of the adrenal that has been isolated in this manner has been shown to be dehydroisoandrosterone a beta kosteroid and is different from the hormone of the testis testosterone an alpha kosteroid. Under certain conditions the beta kosteroids are greatly increased in quantity, as in patients with hyperplasia, adenoma, and carcinoma of the adrenal cortex, and may be of value in diagnosing Cushing's syndrome due to pituitary basophilism from that due to adrenal cortical change.

In the excretion of androgens there appears to be a rather definite relation to the amount of male virilism and with the amount of androgens in the urine. The more marked the symptoms the higher the assay.

Another kosteroid with androgenic action has been isolated from the urine, particularly that by Butler and Marrian (pregnane). This apparently was associated only with that adrenal tumor. The identification of this particular kosteroid required large amounts of urine and with mechanics and talent not available in many laboratories. Its identification was not useful for purposes of preoperative diagnosis.

There is a need of a simple and fairly reliable estimation of all the androgens excreted so that the results may be quickly available to be applied in a survey of the symptoms of each case. It is needed because the symptoms of androgenic excess are more frequent than any other.

Estrogens Frank early called attention to the excretion of large amounts of estrogens in the urine of patients with the adrenogenital syndrome and with virilism. In our former article we called attention to the large or normal amounts so excreted. Slot and Kepler each reported cases in which there was no excess. In the series of Levy, Simpson, de Fremery, and MacBeth, a slight excess of estrogenic hormone occasionally occurred. In our present reported cases we have shown that in young girls with virilism due to a tumor a high amount of estrogens was excreted before the tumor was removed and continued unchanged after removal of the tumor and the virilism had recessed.

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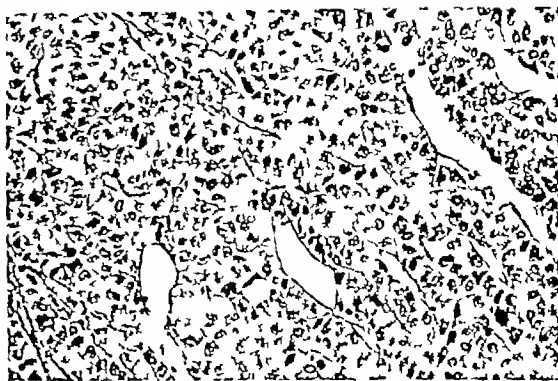


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Fig. 27. Section of tumor removed in Case 6, female with only marked androgenic symptoms. The cells stain deeply, are large in places but not like the nonhormonal male. The cytoplasm contains bandlike granules and also many lipid vacuoles and some foam cells. $\times 60$

We have felt that with both the lumbar and transthoracic route, the operator is too handicapped by the inadequacy of the incision and the impossibility of ligation of the vessels before the tumor is manipulated. It also is impossible to be familiar with the location of the other viscera and vessels from within the limited area above the renal pole. We think that either will give an adequate exposure for small normal or slightly enlarged adrenals. We have had no experience in the bilateral incisions of Young in adults or in cases with tumor. It is satisfactory in children with small hypertrophy of the adrenals and may be with tumor.

The transperitoneal approach that we recommended in our former report has been to us most satisfactory for an adequate exposure and to offer the greatest freedom in proper handling of a tumor especially if it is large. The direction of growth of a tumor of the adrenal is downwards and anterior both in the direction of the incision. The location of other viscera and of the vessels is easier and the reparation of the posterior peritoneum is possible quickly and well. There have been no weaknesses in the abdominal wall subsequent to the operation.

POSTOPERATIVE ACUTE ADRENAL DEFICIENCY

Many cases have been reported with what has been described as shock occurring immediately or shortly following the removal of

an adrenal tumor. Cecil stated that 39 per cent died of this shock and that 66 per cent had severe shock from which 27 per cent of all patients operated upon recovered. The other 33 per cent apparently had no shock.

It is now accepted by most clinicians and investigators that the characteristic collapse is that of acute adrenal cortical deficiency. We have seen this collapse in the removal of a renal carcinoma which invading the adrenal necessitated the adrenal's removal with the perinephritic fat and the tumorous kidney. The collapse terminated fatally and autopsy disclosed that the only metastases from the renal tumor were in the opposite adrenal which had been destroyed. From a perusal of the literature and from our own experience it does not occur in the nonhormonal adrenal cortical tumor cases, or in the pure sex hormonal type cases but occurs in those which show the effects of excess hormonal action upon many metabolic factors: the electrolytes, the water and salt balance, the capillary permeability. In fact the symptoms seen in the Cushing's type whether in children or in adults. It has been advanced on reasonable grounds that in these cases the changes can only be produced by excess hormones. It has been shown experimentally that excess life maintenance substance can cause atrophy of the adrenals. Clinically in those cases ending fatally it has been shown that contra-adrenal atrophy is present with the Cushing type tumors. It has been our experience to have a



Fig. 28. Section of tumor removed in Case 7, female with only androgenic symptoms. The cells are fairly uniform, stain deeply, have anucleated fine granules, and many lipid vacuoles and some foam cells. $\times 60$

patient of this type recover from the adrenal collapse without administration of a potent adrenal extract but later recognition of secreting metastases elsewhere offered the explanation. Broad and Broad reported such a case in which they first attributed the recovery to frequent administrations of adrenaline.

Walters and Kepler stated that the most important factor in surgical therapy of adrenal cortical tumors is the anticipation, prevention, and control of postoperative cortical deficiency. In this we concur but call attention to the mechanism as mostly only occurring in those of Cushing's syndrome, because with the androgenic type tumor there is no functional atrophy of the opposing adrenal.

The method is that used in the crisis of Addison's disease, having on hand and administering preoperatively and postoperatively potent adrenal hormone. A potent extract of the cortex may be used as furnished by Kendall to Walters and Kepler, or desocycorticosterone in adequate doses may be used. In addition to the hormone there is administered by oral or parenteral administration adequate amounts of sodium chloride and sodium citrate. Since the marked cases of Cushing's syndrome have an erythrocytemia, but apparently a marked diminished blood volume, an immediate postoperative transfusion is necessary. It is considered possible that a diet low in potassium might be of value for some time preceding the operation.

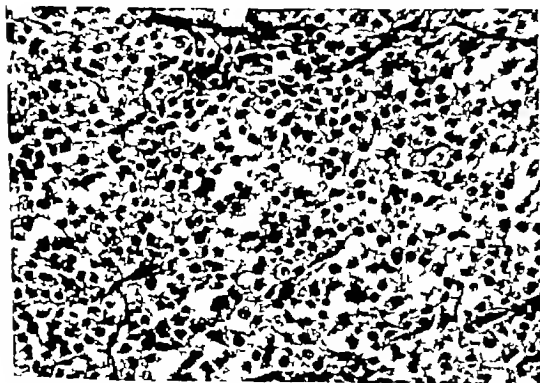


Fig 29 Section of tumor removed in Case 11, a woman with androgenic and Cushing's symptoms. The cells are uniformly of carcinoma, some granules in the cytoplasm, and many lipid vacuoles and foam cells are present. $\times 160$

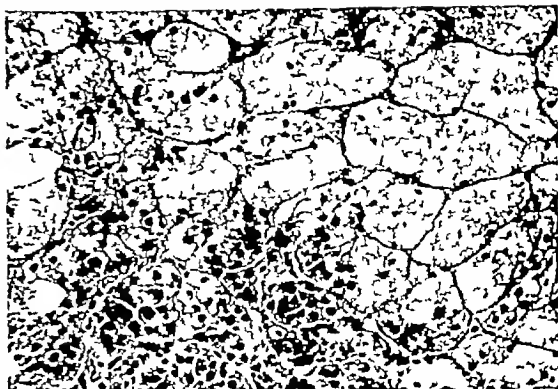


Fig 30 Section of tumor removed in Case 13, a woman with only Cushing's symptoms and no androgenic changes. The entire tumor was composed of huge cells filled with lipid vacuoles, like foam cells. Only in a few places were cells containing granular cytoplasm as is shown in this field. $\times 160$

In 1937 Ingle and Kendall reported that they were able to prevent the atrophy of the adrenals experimentally when large doses of active adrenal cortical substances were given, by the use of an anterior pituitary extract which had high adrenotrophic activity. To date there has been no report as to its effects given preoperatively upon the Cushing syndrome cases, to produce reactivity of the opposing functionless adrenal cells.

Walters and Kepler believe that they have been able to tide the patient over the crisis by replacement therapy and that the remaining adrenal tissue will regain its capacity to produce a sufficient amount of hormones to meet the needs of the body. Since the potent steroid has been available we have not had a marked Cushing's syndrome type tumor, and from our experience, those cases with androgenic changes do not need replacement therapy if an opposing adrenal can be demonstrated by air insufflation x-ray film.

PATHOLOGY

The tumors were either adenoma or carcinoma. The adenomas were soft, encapsulated tumors and histologically did not show any invasive characteristics. The cells were typical of the adrenal cortex of no particular zone and showed lipid vacuoles which compared roughly in number with the degree of hormonal changes.

The carcinomas varied. In the 2 nonhormonal tumors in male adults the cells were frequently of giant size with giant nuclei. They resembled various parts of the adrenal. Lipoid vacuoles were rare. Sections of the specimens obtained from the females without hormonal syndromes again resembled each other. They differed from similar males in the relative rarity of the giant cells and nuclei and the variability of their appearance. At times sheets of cells resembled the glomerular zone; other places the fasciculate; and again the reticulate. In other places they were undifferentiated. They resembled sections of renal hypernephromas. In the cells lipoid vacuoles were infrequent.

Sections of the carcinomas associated with hormonal changes varied. One showed invasion of the capsule and cells in the blood vessels. The cells were in sheets resembling some parts of the adrenal cortex, more frequently the glomerular and reticulate layer. Numerous vacuoles were present. The other had cells mostly undifferentiated with many mitoses and numerous vacuoles present. The number of cell vacuoles against roughly appeared to vary with the amount of hormonal changes.

The more the syndrome approached the Cushing type the more marked was the amount of vacuoles which were present. In the last case with only the syndrome of the Cushing type present, the number of vacuoles present was so great that most of the tumor was composed of foam cells.

In review of our attempts to correlate the finding of fuchsinophilic granules with the symptoms of the disease has still left us unable to decide whether their presence has or has not any particular association with the various types of cases.

Fuchsinophilic staining of the cytoplasm was present in all the tumors, in some diffusely and in others in granules. It apparently was more pronounced in cases with hormonal syndromes.

SUMMARY

1. Adrenal cortical tumors may occur with or without hormonal syndromes or with hormonal syndromes.

2. The hormonal syndromes may be due to an excess of androgens or estrogens or other as yet unidentified hormones.

3. The syndromes are determined by the type and amount of hormone or hormones produced and by the sex and age of the patient.

4. The status of the adrenals may be adequately shown by air insufflation x ray films.

5. Removal of adrenal tumors by the transperitoneal route is surgically best.

6. Acute adrenal deficiency occurs only or mostly in those with symptoms described as Cushing's syndrome.

7. The therapy of this is similar to that which is used in the acute deficiency crisis in Addison's disease.

8. Histologically the tumors that produce the hormonal syndromes have cytoplasmic lipoid vacuoles in amounts comparable to the symptoms.

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The carcinomas varied. In the 2 nonhormonal tumors in male adults the cells were frequently of giant size with giant nuclei. They resembled various parts of the adrenal. Lipoid vacuoles were rare. Sections of the specimens obtained from the females without hormonal syndromes again resembled each other. They differed from similar males in the relative rarity of the giant cells and nuclei and the variability of their appearance. At times sheets of cells resembled the glomerular zone; other places the fasciculate and again the reticulate. In other places they were undifferentiated. They resembled sections of renal hypernephromas. In the cells lipoid vacuoles were infrequent.

Sections of the carcinomas associated with hormonal changes varied. One showed invasion of the capsule and cells in the blood vessels. The cells were in sheets resembling some parts of the adrenal cortex more frequently the glomerular and reticulate layer. Numerous vacuoles were present. The other had cells mostly undifferentiated with many mitoses and numerous vacuoles present. The number of cell vacuoles again roughly appeared to vary with the amount of hormonal changes.

The more the syndrome approached the Cushing type the more marked was the amount of vacuoles which were present. In the last case with only the syndrome of the Cushing type present, the number of vacuoles present was so great that most of the tumor was composed of foam cells.

In review of our attempts to correlate the finding of fuchsinophile granules with the symptoms of the disease has still left us unable to decide whether their presence has or has not any particular association with the various types of cases.

Fuchsinophile staining of the cytoplasm was present in all the tumors, in some diffusely and in others in granules. It apparently was more pronounced in cases with hormonal syndromes.

SUMMARY

1. Adrenal cortical tumors may occur with or without hormonal syndromes or with hormonal syndromes.

2. The hormonal syndromes may be due to an excess of androgens or estrogens or other as yet unidentified hormones.

3. The syndromes are determined by the type and amount of hormone or hormones produced and by the sex and age of the patient.

4. The status of the adrenals may be adequately shown by air insufflation x ray films.

5. Removal of adrenal tumors by the transperitoneal route is surgically best.

6. Acute adrenal deficiency occurs only or mostly in those with symptoms described as Cushing's syndrome.

7. The therapy of this is similar to that which is used in the acute deficiency crisis in Addison's disease.

8. Histologically the tumors that produce the hormonal syndromes have cytoplasmic lipoid vacuoles in amounts comparable to the symptoms.

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the development of anatomic lesions escapes detection and cannot be identified by the senses

Though one does not deny that purely functional phenomena are the predominant pathogenic factors, it is doubtful that they are the only ones, and it becomes less doubtful when one observes cases of evident permanent obstruction to the flow of bile which has lasted for several years and has been controlled only by means of an operation for drainage of bile

Nowadays, in accordance with the modern trend of surgery based on clinical observations at each and every operation one can state by physiological standards that in the presence of any abnormal condition the living body has an anatomic substratum which exists only during life but which either disappears when death takes place or is transformed by death

Hypertrophy of the sphincter of Oddi The occurrence of hypertrophy of the sphincter of Oddi after cholecystectomy has been established beyond doubt by experimental research (Rost). Therefore, it is logical to assume that the same thing occurs in man. It is also logical to believe that hypertrophy is one of the factors producing a resistant papilla. The same phenomenon is frequently found in the cardia and in the rectum, in which the obstructive agent is the sphincter with its marked hypertrophy

It is important to understand that a permanent, real anatomic factor is always added to spasm. The increased amount of contractile tissues about the sphincter, which conflicts with the anatomic and functional conditions of the common bile duct under control of the sphincter, favors the production of stagnation. Similar physiopathological facts are necessarily present in some cases, even in noncholecystectomized patients, because lithiasis in itself creates conditions similar to those which follow cholecystectomy. Moreover, lithiasis is equivalent to cholecystectomy in man. The local edema, hyperemia of the tissues and local congestion, in addition to hypertrophy of the sphincter, will complete the transient sphincteral obstruction or else they will prevent complete closure of the

sphincter in the intervals of muscular relaxation. Infection may be a helpful, although not an indispensable, factor

It is possible that in the 8 cases reported by Strauss the pathogenic mechanism corresponded to the aforementioned physiopathological facts. Strauss' patients complained of pain crises simulating hepatocolic pain without jaundice. At operation it was found that the gall bladder was inflamed but without stones, pericholecystitis was present and the hepatic and common bile ducts were dilated. Cholecystectomy was performed, but shortly afterward the patients suffered attacks similar to those which they had had before operation. A second operation was performed. It was found difficult to insert even a fine catheter through the lumen of the ampulla of Vater which was of increased consistency and the seat of infiltration. The patients were subjected to dilatation of the lumen of the ampulla of Vater, 4 were operated on a third time for recurrence of attacks. This time, choledochoduodenostomy was successful. In some of the patients the ampulla of Vater was the size of a nipple, was red, inflamed, and congested

Anatomic obstruction The more attention one gives to the anatomic obstruction of the sphincter of Oddi the more significant are the clinical observations. A series of cases presenting permanent obstruction at the sphincter of Oddi have been reported during the last few years, by Haberer, Sturm, Melchior, Floercken, and Colp and Doubilet (6). The existence of the anatomic substratum of stenosis of the papilla of Vater in the presence of gall-bladder disease either with or without calculi or concretions is frequent, whereas it is rarely observed at necropsy—a factor which depends on the many changes which take place during life. Physiological conditions may change at any time, a stricture of the duodenal papilla may disappear with the consequent restoration of normal tonus in the sphincter of Oddi as well as the re-establishment of the normal morphology of the biliary tree

Physiological investigations are being carried on with due consideration of the fact that the elimination of bile through the hepatic and

FUNCTIONAL DISTURBANCES OF THE CHOLEDOCHUS AND HEPATIC BILE DUCTS

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IN 1917 surgeons believed that spasm or increased tonicity of the sphincter of Oddi, was the factor which by mechanical action caused biliary pain and jaundice. Shortly afterward, results of experimental research were reported which showed that cholecystectomy is frequently followed by incontinence of the sphincter of Oddi which in turn is followed by muscular hypertrophy of the sphincter as reported by Rost. In 1925 Del Valle reported his observations on obvious structure of the papilla of Vater seen during operation performed on cholecystectomized patients suffering from pain crises.

Further reports of experiments, as well as of findings during operations and of postoperative observations directed the attention of surgeons to the sphincter of Oddi. In 1929 Westphal, Gleichmann and Mann (34) were able to establish that, from a functional point of view the antral upper part of the sphincter of Oddi is vagotonic whereas the lower part is sympathicotonic, as shown by faradic irritation in association with pharmacodynamic substances.

About the same time that functional disturbances in animals were reported I observed by means of operative cholangiography spasms of the sphincter of Oddi in patients whose biliary tract had been operated upon.

In 1930, Nann, Muschel and Pavel reported cases of jaundice due to reflex spasm of the sphincter of Oddi which was classified as functional jaundice. Other cases were reported by Pavel and Jonckheere. More recently several surgeons and research workers, including Walters and Doubilet and Colp (10) observed by means of manometry in addition

to postoperative cholangiography the presence of spasm after the administration of certain substances.

In 1940 I presented before the National Academy of Medicine of Buenos Aires a series of clinical observations and roentgenograms made during the operation which indicated that the existence of abnormal spasm of the hepatic duct was capable of producing biliary stagnation (11).

Method used. I studied the functions of the biliary tree by means of operative cholangiography. The procedure (19) consisted in the majority of cases in injecting through the cystic duct from 3 to 5 cubic centimeters of iodized poppyseed oil at the rate of 1 cubic centimeter a minute. A slow injection is important in order to prevent a sudden distention of the biliary tree. By this method the operation is performed under the best physiological conditions; the registered phenomena can be correctly interpreted and, at the same time the pathological conditions can be clearly differentiated from the normal. Up to the present, this study includes 800 cases of biliary lithiasis which have been systematically observed by means of operative cholangiography.

THE SPHINCTER OF ODDI

The majority of surgeons believe that a more or less prolonged spasm of the sphincter of Oddi is the only cause of biliary stagnation. They believe that the free flow of bile is obstructed by the increased tonicity of the sphincter; the intensity and rhythm of which are controlled by several factors, in particular by diseases of the gall bladder and concretions.

The Chinese aphorism "the sum of the parts is not the total" can be applied to the field of medicine. The functional factor which according to Bergmann is the *primum moriens* in

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Niessen, 27), "dyssynergia of the common bile duct" (Best and Hicken), "biliary dyskinesia" (Ivy), "papillitis," "sphincteritis" (Walters), "resistance of Vater's papilla," "scleroretractile choledochodditis" (Del Valle)

Classification Any extreme classification will be either insufficient or exaggerated. I believe that the term "odditis" for all the phenomena of obstruction will properly cover the field. Odditis is then divided into dystonia and stenotic odditis.

Dystonia is evidently exhibited as a functional disorder—there is incomplete closure of the sphincter due to spasm in the distal sympatheticotrophic part of the sphincter only. This functional disturbance causes a reflux toward the duct of Wirsung. The phenomenon must occur in a larger number of cases than is shown by operative cholangiography. The two ducts do not open into the ampulla of Vater in all cases, and also it may not be possible to detect the phenomenon in the operative cholangiogram (see Fig. 3). Dystonia may be compared with the type of dysthyroidism of the dualists, whereas early stenotic odditis may be compared to hyperthyroidism. The former is due to a dissociated function, whereas the latter is due to an increased one. Therefore, the name dystonia is proper for that functional disorder.

Stenotic odditis is a term applied to any type of resistance of the ampulla of Vater without specifying the causes of the more or less permanent obstruction at the sphincteral segment. In some cases the resistance is due to true total hypertonicity of the sphincter of Oddi. Sclerotic retraction occurs only in rare cases.

Now then, operative cholangiography deals with the problems of the various types of dystonia and stenotic odditis with an essentially physiological criterion. Moreover it fulfills all the requirements necessary to reduce the causes of error to a minimum. The injection of the opaque substance is made slowly and in very small amounts, thus distention of the bile ducts and the entrance of foreign matter in the hepatobiliary system are prevented and the anatomic integrity of the ducts

is well preserved. The main objection to the use of large doses of opaque substance is that such doses provoke phenomena of spasm and thus facilitate the immediate entrance of the injection material into Wirsung's duct. This occurrence may lead the surgeon to believe that there are biliary disturbances present. The latter can also be erroneously suspected from the enormous dilatation of the biliary tree which was caused by the injection but which can be wrongly interpreted as being caused by stagnation. Examination of the bile ducts through a fistula or with a T-shaped tube should be even more severely criticized. Choledochotomy, the presence of a tube in the lumen of a delicate duct, the increased pressure, and the large dose of opaque substance in the bile ducts are factors which necessarily disturb the physiology of the ducts and modify their morphology.

Dystonia In accordance with the hypothetical statement previously made concerning the normal physiology of the hepatobiliary system, the common bile duct evacuates its contents through the papilla of Vater while in relaxation. Any factor which partially disturbs the contractile mechanism of the papilla produces dystonia, which may be compared with experimental hypotonic stagnation (Westphal) provoked by the contraction of the sympatheticotrophic portion of the sphincter of Oddi. Quick entrance of the opaque substance (lipiodol) into the duct of Wirsung during operative cholangiography is a clear indication of dystonia. It is possible that in a certain number of cases transient spasms of a dissociated character are not noticeable during the operation because of the lack of reflux into the pancreatic duct, due to the absence of the ampulla of Vater. Cases of this type, under the circumstances, are therefore included in the group of stenosing odditis. In our series 4 per cent of cases were classified as dystonia.

Some investigators (Desplas, Moulounguet, and Malgras) believe that the entrance of an opaque substance into the duct of Wirsung has no pathological significance. They are led to this conclusion because of their method of carrying out the operation: the injection into the gall bladder or into the common bile duct

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common bile ducts is the explanation of the harmoniously co-ordinated functions in which peristalsis of the common bile duct, contraction of the hepatic duct, and the tonus of the sphincter of Oddi are equally important. From pathogenic and physiological angles, a papilla of Vater of normal patency in the presence of hypertrophy of the common bile duct constitutes a more or less evident obstacle to the papilla. Dilatation of the biliary tract indicates a functional disturbance even in the absence of any anatomic lesion. A spastic hypertonic papilla in a choledochus with normal tonus is also an obstacle against which the duct reacts with detrimental effect to its energy and muscular ability, thus producing dilatation of its lumen and elongation and sinuosity of the duct.

The study of transverse sections of the distal choledochal segment including the sphincter of Oddi revealed in 50 per cent of the cases of lithiasis evident muscular hyperplasia, especially annular hyperplasia, and a moderate hyperplasia of the longitudinal and oblique muscular fibers.

Muscular hyperplasia was so great in these cases that after further evolution, it caused the limiting zone between the muscular rings of the sphincter to disappear. Increase of the connective tissue was also observed in some cases, especially in those in which muscular hyperplasia did not occur. Increase of both the muscular and connective tissues occurred in some cases (Westphal 33). These anatomic changes may take place in the choledochal segments of the sphincter of Oddi, even though the common bile duct does not contain stones.

Choledochitis and anatomic obstruction of the papilla of Vater. In 1908 surgeons of the French school, especially Gosset, discussed before the Congress of Surgery in Paris the rôle of stenotic and nonstenotic inflammation of the common bile duct without stones in the production of biliary stagnation and in the development of jaundice. Later Charrier and Thalheimer, also surgeons of the French school, reported their observations in 27 cases of choledochitis without concretions and described the lesions which were observed in the common bile duct, the hepatic duct, the gall

bladder and the pancreas. A group of cases of choledochitis which is secondary to cholecystitis and biliary stagnation and which follows the evolution of these conditions, is clearly differentiable in the 27 cases. The appearance of the common bile duct in some cases of this group resembles a pipe (the so called *tuyau de pipe* of French surgeons). The lumen of the duct becomes narrower with each recurrence of the inflammation until finally it is so small that even a fine probe cannot pass through. In such cases, the phenomena of biliary stagnation are aggravated by the spasm of the sphincter of Oddi. Choledochitis is an added factor of irritation (Brocq). Cases of either partial or diffuse inflammation of the common bile duct constitute a group of surgical cases of choledochitis in which interstitial sclerosis involves not only the walls of the duct but those of the ampulla of Vater as well (Chabrol and Klots).

Argentinean surgeons, especially Del Valle, called attention to a group of cholecystectomized patients who had been operated on for the so called choledochal syndrome, namely hepatocolic pain. Oddi's sphincter was stenotic (retractile choledochododitis). The process of inflammation was verified by microscopic studies. I have in my files the record of a case of choledochitis with stricture of the papilla of Vater. A brief résumé of the record follows.

Series 1. Case 24. A woman, aged 4 years, suffered from repeated attacks of hepatic pain and jaundice which were over as quickly as they appeared. A enlarged gall bladder (the size of duck egg), 5 centimeters in length without tones and with thick walls, was surgically removed. The cystic duct was in free communication with the common bile duct, which was like rigid tube the size of the little finger. Its walls were 2 millimeters thick. A fracture of the ampulla of Vater and the absence of calculi were disclosed by means of operative cholangiography. Papillary fibrous stricture was found during duodenostomy. The ampulla of Vater was incised. The patient recovered.

Nomenclature. The names applied to the alterations in the sphincter segment of the common bile duct vary widely because of the lack of consistency in the understanding of their etiology and pathogenesis. They include spastic cholepathy (Schmieden and

Niessen, 27), "dysnergia of the common bile duct" (Best and Hicken), "biliary dyskinesia" (Ivy), "papillitis," "sphincteritis" (Walters), "resistance of Vater's papilla," "scleroretractile choledochododditis" (Del Valle)

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of a large dose of the opaque substance with increased pressure sometimes through a fistula or by means of a drain tube.

The circumstances under which operative cholangiography is performed vary, and one may conclude that the flow of the opaque material into the duct of Wirsung when not caused or provoked by a defective method of injection is far from being a mechanical and passive phenomenon. One is convinced that the flow into Wirsung's duct is an active phenomenon which is caused by the current of the biliary tree flowing into the pancreatic tree. This would seem to indicate that at certain times the current flows in an opposite direction, namely from Wirsung's duct to the biliary tree. Several factors indicate that the entrance into Wirsung's duct is an abnormal active phenomenon of pathological significance which might explain the disturbed function (dystonia). Some of these factors are:

1. The unmistakable evidence during observation of the two different phases, namely in the first phase total closure of the ampulla of Vater and in the second phase partial opening of the ampulla with persistence of the sympathicotonic ring of Oddi's sphincter by which the flow of the opaque substance into Wirsung's duct is permitted (Figs. 1 and 2).

2. The fact that in certain cases the opaque substance may be seen in the first film occupying only the terminal segment of Wirsung's duct and, shortly after the substance may be observed filling the entire duct (Figs. 3 and 4).

3. The contour of the duct is modified by pre-existing stagnation. The duct looks sinuous, dilated and increased in diameter. The fusiform dilatation of the segment of the duct near the ampulla of Vater indicates that the excretory functions of the duct are pathological. The ampulliform aspect of the terminal segment of the duct is the most evident proof of stagnation which little by little modifies the architecture of the duct at the part where it opens into the ampulla of Vater (Figs. 2 and 5).

4. The associated lesions and the further progress of the disease, as observed in a group

of patients with dystonia, seemed to indicate intimate relations between the two excretory systems. Cholecystitis dissecans, also called exfoliative cholecystitis, was present in 1 case. In another case the presence of a calculus and reflux into Wirsung's duct were observed during operative cholangiography (Fig. 5). In this case Kehr drainage was applied and the fistula healed well. Later however the common bile duct ruptured with consequent choleperitoneum. In other patients not properly treated for stagnation the crises of pain recurred repeatedly as a result of functional disturbances and the patients had to submit to other operations.

ROENTGEN ASPECTS

Dystonia. The retention of injected material in the pancreatic duct is transient. Within a few minutes, when the sphincter is in complete relaxation the duct empties its contents at the same time that the contents of the biliary tree are evacuated. The duct of Wirsung in the cholangiograms appears sinuous, dilated and moniliform, that is, it has a morphological aspect which indicates repeated increased tension on the duct, both because of the stagnation of the pancreatic secretion and because of the reflux of bile. In cases of dystonia, the biliary tree is somewhat dilated and sometimes elongated and sinuous as a result of biliary stagnation. In some cases, it may be observed that the biliary and the pancreatic trees form at times one united system as they meet at the level of the ampulla of Vater.

Inflammatory stenosis of the sphincter of Oddi. Stenosing odditis varies in intensity from simple hypertonicity to complete obstruction of the sphincter of Oddi. The former is comparable to experimental hypertonic cholechohal stagnation (Westphal); the latter depends on anatomic factors such as retractile sclerosis (Del Valle). My personal statistics give an average frequency of 1 per cent.

Stenosing odditis is identified by the stagnation of the opaque substance into the biliary tree 15 or 20 minutes after having been injected into the tree.

The contour of the ampulla of Vater is the most varied. It may be similar to the 'sharp

end of a pencil," "hookshaped," or in "the form of the tip of the finger" In most cases a small amount of opaque substance passes into the duodenum The whole biliary tree, down to the finest intrahepatic branches, appears in the different films throughout the operation The common bile duct is flexuose, elongated, and of an increased diameter It is almost always in active peristalsis, as shown by the undulations of its contour In some cases a general atony of the whole biliary tree may be observed

In the roentgenograms, the main structures for the excretion of bile present functional and morphologic aspects which indicate their constant strain against the resistance of the sphincter

RESULTS OF THE DISTURBANCES OF THE SPHINCTER OF ODDI

The functional sphincteral disturbances little by little cause anatomic lesions of the pancreas and of the biliary tree The cholangiograms in my own files show how frequently lipiodol enters the pancreatic duct, a result especially favored by dystonia I believe that biliary lithiasis, and particularly the functional disorders caused by the disease, predispose to the development of acute necrosis of the pancreas The fact that in a large majority of cases chronic pancreatitis is a sequela to biliary lithiasis supports my belief Dystonia may be revealed by operative cholangiography in 3 per cent of the cases In many of these cases the roentgenograms reveal the duct of Wirsung in its full extent Frequently its diameter is increased, a condition which proves that previous stagnation has been present By means of these operative observations, which prove beyond doubt the existence of functional disturbances in the main excretory route of the bile, it becomes easy to understand how such disturbances favor the entrance of bile into Wirsung's duct The disturbance in function is sufficient again and again to cause the establishment of communication between the common bile duct and the pancreatic duct These functional disturbances cannot be felt on palpation nor seen by the eye And yet, they become so marked that at times the diseased condition

of the gall bladder (cholecystitis) is disguised by the associated lesions of the biliary tract and pancreas

The reflux of bile into the pancreatic tree creates in itself an abnormal condition which is dangerous to the anatomic integrity of the pancreas The injection of from 30 to 60 cubic centimeters of serum into Wirsung's duct have been considered harmless because they do not cause macroscopic lesions (Estrade) There is no doubt, however, that they do cause anatomopathological lesions from internal trauma, tearing the fine pancreatic ducts and causing foci of glandular necrosis (Brocq)

The most complete statistical records of the past few years show that acute necrosis of the pancreas is a predominant complication of biliary lithiasis—a factor which proves the important relation between the two diseases (Schmieden, 28)

On the other hand, it cannot be denied that a calculus in any part of the common bile duct, especially in the ampulla of Vater, causes irritation which in turn favors spasm The stone provokes evident dystonia of the sphincter In several instances calculi have been found impacted in the ampulla of Vater during necropsy in the presence of pancreatic necrosis

In the Museum of Pathologic Anatomy I saw such an anatomic specimen (Ferraris), which had been taken from the body of an old man who died from pancreatic necrosis The calculus, the size of a gram of wheat, was impacted in the ampulla of Vater and the sharp end of it entered the lumen of the duodenum

It is also important to direct attention to the frequency with which acute pancreatic disorders are observed in vagotonic patients In 48 necropsies following death from pancreatic disease, biliary lithiasis was found in 28 instances In 10 of these the biliary tree did not show anatomic changes but the history showed justification for a presumptive diagnosis of neurosympathetic disorders (Stocker) All the aforementioned findings indicate the important rôle which the ampulla of Vater plays in the pathogenesis of diseases of the pancreas

Now then, the functional disturbances which follow reflux of pancreatic ferments evidently play an important part in the evolution of cholecystitis and in the pathogenesis of choledochitis. Certain factors observed in my patients indicate that in some cases pancreatic ferments play an important rôle in perforation of the gall bladder. The reflux of pancreatic juice into the bile ducts is a proved fact. However it becomes of pathological significance only when it occurs in the presence of sustained blockage of the bile ducts and in association with other factors which activate trypsin. Because of the blockage a large quantity of pancreatic juice enters into the gall bladder. The vesicular bile normally acid, becomes alkaline while at the same time the ferments are activated by the action of the infected bile (Colp, Doubilet and Gerber 7).

On the other hand the fact is emphasized that the peculiar character of exfoliative and dissectant cholecystitis (23) depends on the action of the pancreatic ferments during their reflux into the common bile duct and the gall bladder. The reflux is favored both by dys-tonia of the sphincter of Oddi and by the great pressure of the juice in the pancreatic tree, which is higher than that of the bile in the biliary tree (Harms).

The general structure of the tunicae of the gall bladder which constitute the necrotic sac in these cases, can be identified by microscopic study because of the fact that the changes in the elastic and connective tissues are not marked notwithstanding the presence of great changes in the structure. This fact, which is of great pathogenic significance indicates that the lesions are caused by digestive ferments since the gangrene and suppuration which are caused by infection destroy the tissue structure to such an extent that it cannot be identified especially if there are vascular lesions which diminish the vitality and resistance of the tissues.

The reflux of pancreatic ferments most likely will play an important part in the production and development of choledochitis. It has been proved by experiments (Westphal) that besides choledochitis of the necrotic type followed by biliary peritonitis there can be

produced chronic, productive inflammation with destruction of the elastic tissues of the wall of the common bile duct and dilatation of the duct.

HEPATIC DUCT

Before a meeting of the Academy of Medicine of Buenos Aires, which was held October 22 1937 with Professor B. Houmay as chairman, I presented my observations on the physiopathology of the extrahepatic bile ducts as seen by means of the operative cholangiography. I directed attention to certain phenomena which I had observed and which indicated that there really is a contractile mechanism namely a physiological sphincter at the level of the hepatic duct (20). Normal contraction of the sphincter separates the intrahepatic bile ducts from the extrahepatic branches of the biliary tree at times during normal elimination of bile. However in the course of diseases of either the intrahepatic or the extrahepatic branches of the biliary tree the contractile sphincteral functions are disturbed to such a degree that one is justified in establishing the presence of a pathological process in the hepatic duct and its branches.

FUNCTIONAL SYNDROMES

A functional disturbance in the contraction of the sphincter of the hepatic duct prevents synergic action between the duct and other parts of the entire system of elimination of bile. From the knowledge gained by operative cholangiography it is evident that the disorder of sphincteral contraction is an important factor in the production of pain and of biliary stagnation.

CASE 2. (No. 5 of series 6.) L. F. aged 31 years, was admitted to the hospital in October 1937. She had had several attacks of typical biliary pain during the last few months before entering the hospital. She exhibited signs of myocarditis for which she had the proper treatment.

At operation chronic calculous cholecystitis was found. The patent cystic duct in the form of band crossed the main root of the biliary excretion at the front and opened into the internal border of the retroduodenal segment.

Operative cholangiography as performed. The first film after injection through the cystic duct showed the system of the hepatic duct to be rather dilated and injected. During operation the normal course of the cystic duct and the opening of the duct into segment lower than that in which the



Fig 1 Dystonia of the sphincter of Oddi. Total closure of the ampulla of Vater. The injection of 3 cubic centimeters of lipiodol was made through the cystic duct, *Cs*. The system of the hepatic duct, *H*, contains lipiodol. The common bile duct, *C*, with dilated and undulated contours does not evacuate its contents into the duodenum because of total closure of the ampulla of Vater, *P*.

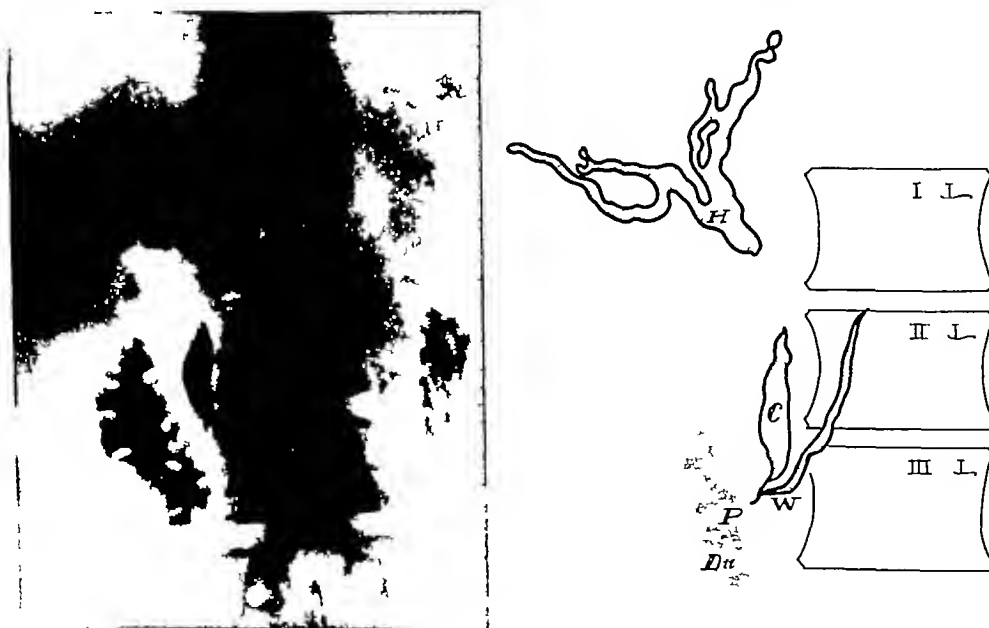


Fig 2 Roentgenogram of same patient as in Figure 1 taken 10 minutes later showing partial closure of the ampulla of Vater. The system of the hepatic duct, *H*, contains lipiodol. The common bile duct, *C*, has evacuated a portion of its content of lipiodol into the duodenum, *Du*, through the ampulla of Vater *P*. Lipiodol has flowed into the duct of Wirsung, *W*, the terminal segment of which is ampulliform.

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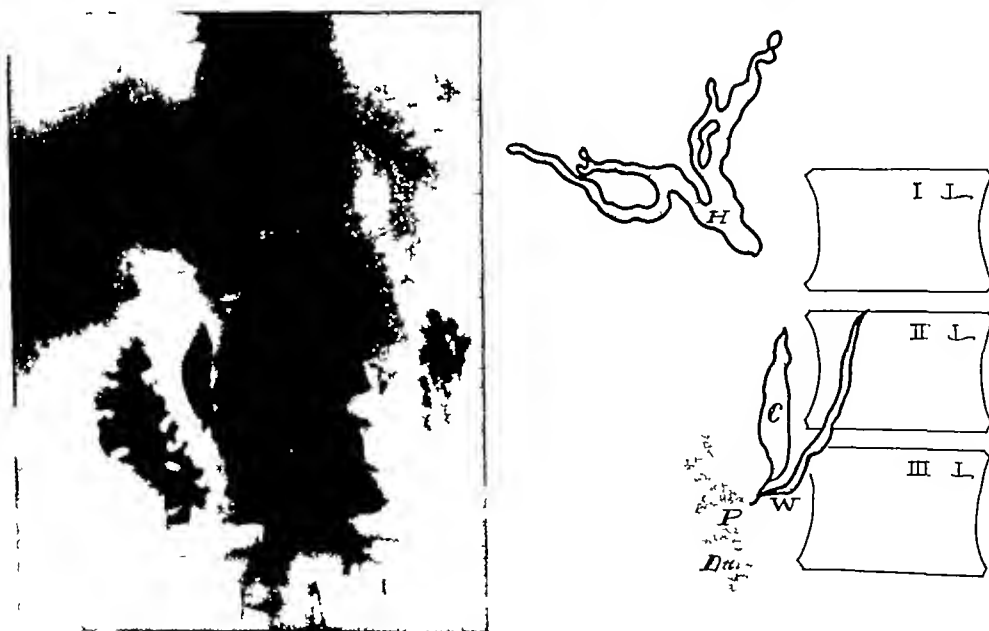


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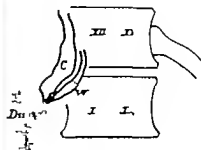


Fig. 3. Dystonia of the sphincter of Oddi. The injection of lipiodol, as made into the cystic duct. The common bile duct, C, contains lipiodol, Wirsung's duct, W, which is injected in its terminal segment, does not show because of its proximity to the lumen of the common bile duct. A little opaque substance has passed into the duodenum.

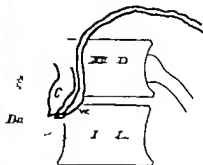


Fig. 4. Roentgenogram obtained minutes later than that in Figure 3. Lipiodol has flowed in greater quantity into the duct of Wirsung, W, which is visible in its entirety.

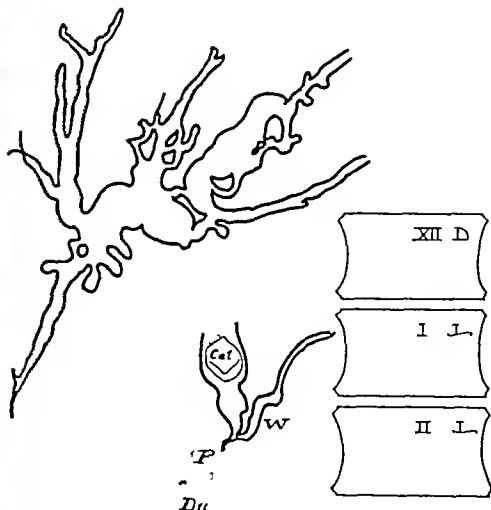


Fig 5 Dystonia and choledocholithiasis. The injection of lipiodol was made through the cystic duct. The intrahepatic biliary tree is dilated and filled with opaque substance. The terminal third of the common bile duct, C, contains a smooth stone Cal, lipiodol has flowed into the duct of Wirsung, W, the terminal segment of which is visible, undulated, ampulliform. A small quantity of lipiodol has passed through the ampulla of Vater, P, to the duodenum.

duct normally opens were verified. The common bile duct, increased in diameter, was visible. A little lipiodol passed into the duodenum. The second film showed that the system of the hepatic duct was still injected. An accessory hepatic duct was identified. The diameter of the common bile duct was seen to have been reduced and the duct had evacuated almost all of its contents of opaque substance into the duodenum.

The first film indicates that retention of the opaque substance in the intrahepatic branches of the biliary tree depends on the transient action of an active obstructive factor at the level of the hepatic duct. The injection of the accessory duct could be explained by no other mechanism of action than this. The contraction of the upper part of the biliary tree was not sufficient at a given time to overcome the

resistance of the contracted hepatic duct. Moreover, it caused reflux of the opaque substance into the accessory hepatic duct which opened above the contracted segment of the hepatic duct. The phenomenon, in this case, is similar to that which occurs when the sympatheticotrophic part of the sphincter of Oddi is in contraction from dystonia and reflux into the duct of Wirsung takes place.

CASE 2 (No 7 of series 43) C M de P, aged 55 years, was an obese multiparous woman. Three years before she had suffered acute pain in the epigastric region, with nausea and vomiting spells. The attack was followed by jaundice and discoloration of feces for about 2 months. The crises of pain recurred at intervals.

Operation was performed May 30, 1940. The subhepatic space was blocked by strong adhesions.



Fig. 6. Functional syndrome of the hepatic duct. Roentgenogram taken 15 minutes after the injection. The hepatic duct system, *H*, is completely filled with the substance. Contraction of the distal segment of the hepatic duct (indicated by arrow) is the obstruction. The common bile duct, *C*, of almost normal diameter with repeated peristaltic movements makes lipiodol flow into the duodenum, *D*, through the ampulla of Vater, *P*. The opaque substance contained in the duct of Wirsung, *W*, is visible in the terminal third of the duct.

with the colon and the duodenum. The gall bladder had been reduced to fibrous nucleus. The findings seemed to indicate that the structure had previously been in communication with the intestine through fistula which had healed. During dissection the cystic duct had been cut at the level of the common bile duct.

Operative cholangiography was carried out but because the cystic duct was missing it was necessary to inject the opaque substance directly into the common bile duct. The injection had to be made faster than usual because of the reflux of the substance over the lateral surfaces of the cannula.

The injection seemed to cause signs of dilatation or very anatomic disturbance of the common bile duct because of adhesions between the hilus of the liver and the neighboring structures. Therefore, 8 cubic centimeters of lipiodol was injected, or a dose almost three times that customarily used when the common bile duct is normal. The possible presence of a mechanical obstruction which as produced by calculi or some other cause as kept in mind because of the fact that jaundice had been present for so long time.

The rapid injection of the large doses caused distention of the biliary tree and spasms. The system of the hepatic duct appeared to be engorged with the

substance and the duct as strongly contracted. The diameter of the common bile duct was slightly increased and was peristaltic. The duct of Wirsung was filled with the substance. The ampulla of Vater had relaxed to allow passage of the opaque substance.

In the second film, obtained 15 minutes later the findings are the same with slight variation namely the diameter of the common bile duct was reduced to normal, whereas the hepatic duct was distended above its distal segment which was in marked spasm (Fig. 6).

The results which follow the sudden distention of the biliary tree when the walls of the bile ducts are elastic and irritable are plainly shown by the aforementioned findings. These findings prove also that the circumscribed spasm of the distal segment of the hepatic duct causes more or less prolonged stagnation of the contents of the intrahepatic bile ducts. It is evident then that spasm of the hepatic duct causes slow progressive dilatation of the intrahepatic branches with consequent stagnation—the predominant patho-

genic factor of both transient jaundice and hepatic pain

Similar phenomena have been observed in several patients with subintrahepatic crises. The distention of the system of the hepatic duct, due to prolonged contraction of the duct which was verified in these patients, was the only explanation for the almost continuous hepatic pain. Neither the gall bladder nor the sphincter of Oddi played any part as causal agents. As seen by operative cholangiography, the gall bladder was in retractile sclerosis and deprived of all its functions of contractility. The cystic duct was obstructed, the sphincter of Oddi did not disclose any obstacle at the level of the ampulla of Vater. Now, by studying by means of operative cholangiography the association between the pathological anatomy and the clinical pathology and the function of the main route of elimination of bile, we have obtained sufficient data to support the statement that the hepatic duct system plays a most important part in the pathogenesis of hepatocolic pain.

SUMMARY AND CONCLUSIONS

1 The disturbances of the sphincter of Oddi are functional in a great majority of cases. The interference by a permanent, stenosing, anatomic factor are found to be rare.

2 Anatomic stricture of the ampulla of Vater is frequently associated with indurated thickening of the common bile duct (choledochitis).

3 The reflux of lipiodol into the duct of Wirsung is a characteristic roentgenographic finding in the presence of dystonia of the sphincter of Oddi. It represents a pathological phenomenon.

4 Functional disturbances in the sphincter of Oddi in association with reflux into the pancreatic duct are the cause of anatomic changes in both the pancreas and the biliary tract.

5 Functional disturbances in the hepatic duct may occur. In some cases the disturbances are the cause of the development of transient jaundice. The functional disorders of the hepatic duct in association with distention of its branches are quite frequently the

pathogenic factors which are involved in hepatic colic.

6 Roentgenograms and clinical proof of my theory stated herein were recently presented (22) in Buenos Aires, with the following conclusion: "In summarizing, *a posteriori*, without divorcing our belief from the general conception of the development, type, and course of biliary pain, it is evident that such a condition in which the factors of obstacle and infection play a rôle in varying proportions (Sprengel) is different in every patient. The degree of intensity varies with the individual because, as Leriche says, pain is like a lamp in an electric circuit, the glow and intensity of its light depending on the intensity of the electric current which passes through its circuit. Therefore there is no doubt that biliary pain, from a pathogenic point of view, is often a functional syndrome of the system of the hepatic duct only to which disturbances of the pancreatic tree, originating in dystonia of Oddi's sphincter, are sometimes added."

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THE TREATMENT OF EXPERIMENTAL SHOCK BY THE INTRAVENOUS INJECTION OF DILUTE, NORMAL, AND CONCENTRATED PLASMA

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THE treatment of traumatic shock demands the restoration of the depleted effective circulating blood volume. Large amounts of fluid and plasma protein are lost from the circulation, and these elements must both be replaced in the relative proportion that they have been lost. When dogs are shocked by intestinal trauma, the fluid which is lost from the peritoneal surfaces contains 3 to 4 per cent protein. This type of shock can be most efficiently treated by restoring to the circulation large amounts of half dilution plasma containing the same proportion of protein that has been lost. Treatment with more concentrated plasma solutions is less effective. The value of half dilution plasma in the clinical treatment of shock has been emphasized in a previous publication (10) and this finding conforms with the experimental results which are being reported elsewhere in the literature.

The widespread recognition of the value of plasma in the treatment of shock has been attested by the numerous publications discussing this subject during the past 2 years. The rapidly accumulating clinical experience, both in this country and in England, has established its efficacy in combating the shock resulting from hemorrhage, trauma, or burns. Plasma finds its greatest value in shock associated with a preponderant loss of the liquid elements in the blood, but it is also of unquestionable value in the emergency treatment of hemorrhage (3). Blood plasma may be preserved in the liquid form for a limited period, or in the lyophilic, or dry form, for an indefinite time. The various papers discussing the use of plas-

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ma in shock have not been concerned primarily with the concentration to be injected. Elsever has used dilute plasma, but the most commonly used form has been whole plasma. Hill (8, 9) and his coworkers have advocated the use of 4 times concentrated plasma in both the prophylactic and therapeutic treatment of shock. This departure from the more common methods of treatment is strikingly convenient, but depends on the presence of available body water to restore the circulating blood volume.

The recognition that the diminished blood volume is one of the fundamental principles of shock has led to an exhaustive search for the method of its development and the location of the fluid lost. The theory of traumatic toxemia (Cannon) postulates a generalized capillary permeability resulting from a toxic product elaborated at the site of trauma. The importance of local fluid loss at the site of trauma was emphasized by Blalock and by Phemister, who produced shock by traumatizing the extremities of dogs. A tremendous amount has been written since that time, and it is clearly evident that many factors are concerned. These vary from the process involved after a simple hemorrhage from an artery to the complicated mechanism developing after a penetrating wound of the abdomen with minor bleeding. The rôle of the sympathetic nervous system (Freeman), the rôle of visceral capillary dilation (Moon) and that of potassium (Scudder) are all factors in the mechanism of fluid loss, but individually they do not appear to furnish adequate explanation. The increasing information regarding circulatory mechanics, water balance and electrolytes, endocrine dysfunction, and anoxia will eventually be correlated in a more concise understanding of the shock mechanisms.

TABLE I—THE BLOOD VALUES IN A CONTROL EXPERIMENT—DOG 40-333, WEIGHT 10.6 KILOGRAMS

	Hb vol	Ht vol c.	Hemato- crit cent	Spindle protein	Plasma protein concentration per cent	Albumin concentration per cent	Globulin concentration per cent	Total protein per cent
Dog 40-333 W. 10.6 kg Control	490	530	42	0.767	9.6	6.1	4.4	9.5
hr after trauma	490	1060	44	0.8				3.1
hr after trauma	493		49	0.733	15		6.1	19
hr after trauma	477	85	37.4	0.734	13.5		6.6	

EXPERIMENTAL METHODS

Dogs weighing from 15 to 25 kilograms were used in all of the experiments and shock was produced by peritoneal trauma under nembutal anesthesia. A typical experiment was performed in the following manner. The dog did not receive food on the evening before, but was given water *ad lib*. On the morning of the experiment it was given 0.08 gram of morphine subcutaneously and half an hour later sufficient veterinary nembutal intravenously to produce narcosis. This method of administration was found to be the most satisfactory because of the great variation in the tolerance of the individual animal to nembutal. The control plasma volume was determined after one half hour of anesthesia, when the animal could be considered to have reached a basal level. The femoral artery was then cannulated and attached to a recording mercury manometer. The blood pressure tracing was recorded on a smoked drum. Blood sam-

ples were taken by jugular venipuncture with an 18 gauge needle without hemostasis except when the venous pressure was very low. The peritoneal cavity was exposed through a midline incision with careful hemostasis. The entire small bowel from the duodenum to the cecum was delivered and gently traumatized with a flat blade retractor. The bowel was held between the fingers and a uniform blow was delivered on the antimesenteric surface. It was necessary to repeat the trauma a second time when dealing with larger dogs. The fluid which exuded from the traumatized bowel was collected extraperitoneally and the bowel was covered with oiled silk to prevent evaporation. Plasma was injected intravenously by gravity and a Murphy drop bulb was inserted in the system to regulate the flow at 40 to 45 drops per minute.

Blood plasma was injected in three different concentrations, that is, as whole undiluted plasma, as one half dilution plasma, and as a

TABLE II—A COMPARISON OF THE BLOOD VALUES WITHOUT ANESTHESIA, WITH NEMBUTAL ANESTHESIA ALONE, AND AFTER TRAUMA

Plasma volume	Blood volume	Hematocrit	Total protein concentration	Total albumin concentration	Total globulin concentration	Total circulating protein	Total circulating albumin	Total circulating globulin	Remarks
							17		Control without anesthesia
	18					19		+	Control with anesthesia
26	26.8	—21	—	28	—46 (51 gm)	—47 (50 gm)	—45 (51 gm)	—45 (50 gm)	Shock—retained trauma
29	—29	—	29	26	—47 (50 gm)	—47 (50 gm)	—45 (50 gm)	—45 (50 gm)	Shock—retained trauma
29	—	+24	—	—	—48 (52 gm)	—47 (50 gm)	—45 (51 gm)	—45 (51 gm)	Shock—retained trauma
44	41	—24	23	—	—45 (50 gm)	—45 (50 gm)	—45 (50 gm)	—45 (50 gm)	Shock—retained trauma
47	44.5	+30	—	—	—44 (51 gm)	—44 (50 gm)	—45 (50 gm)	—45 (50 gm)	Shock—retained trauma
33	+	—	—	8	—44 (51 gm)	—47 (50 gm)	—45 (50 gm)	—45 (50 gm)	Shock—retained trauma

times concentrated plasma The half dilution was prepared by adding an equal volume of normal saline to whole plasma, and the 4 times concentrated by redissolving lyophile plasma in one-fourth the original volume of distilled water The prophylactic and therapeutic efficacy of these solutions was tested The prophylactic injection was started coincident with the trauma, the therapeutic injection was not started until the blood pressure had fallen below 80 millimeters of mercury

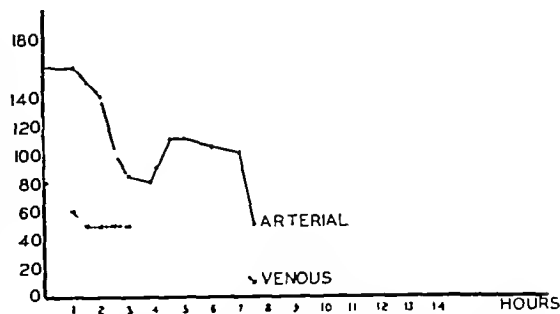
The volume of dilute and whole plasma injected corresponded to the dog's circulating plasma volume The prophylactic effect of 4 times concentrated plasma was tested with correspondingly large volumes The therapeutic effect was determined with the smaller amounts which have been suggested for clinical use

The peritoneal fluid was collected during the experiment and its protein content determined The animals were killed at the close of the experiment, and sections of the various organs were removed for microscopic study

Repeated observations were made of the arterial pressure, venous pressure, and circulation time Blood samples were collected in dry potassium oxalate (2 mgm /c c of blood) for determination of the hematocrit, plasma specific gravity, total protein concentration, albumin, and globulin The circulation time was determined by the sodium cyanide method (4) The protein concentration was determined by the micro-Kjeldahl method, and the albumin globulin ratio by Howe's method The gravimetric pipette was used in the determinations of specific gravity (4) The plasma volume was obtained by the direct blue dye method of Gibson and Evans, the spectrophotometer being used Correction for hemoglobin was made The accuracy of plasma volume determinations may well be questioned when the circulation is failing and the hematocrit is 50 per cent or more For this reason, only gross changes in volume have been considered significant

EXPERIMENTAL OBSERVATIONS

The typical reaction of a dog to trauma of the bowel is indicated in Graph 1 There is a primary fall in the arterial blood pressure



Graph 1 Control experiment Arterial and venous blood pressure in shock produced by intestinal trauma

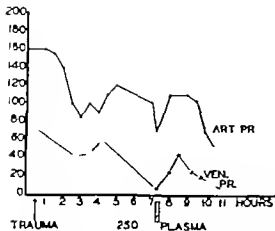
during the first 2 or 3 hours of the experiment followed, in most cases, by a temporary secondary rise The blood pressure then gradually falls until the animal displays the typical signs of profound shock with peripheral circulatory failure

The time required after trauma for the blood pressure to fall and the survival time vary considerably in different animals The survival time averaged 8 hours, varying from 5 to 12 hours

The pulse rate is usually rapid and regular during the early hours of the experiment, but frequently decreases with the appearance of severe shock The venous pressure slowly declines and in profound shock it is impossible to withdraw blood from the veins

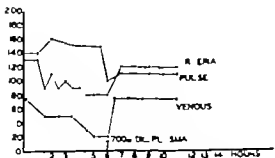
The blood findings in a typical control experiment are outlined in Table I The plasma volume slowly decreases throughout the experiment, with a parallel change in the total blood volume The change is less marked in the red cell volume calculated from the hematocrit, which indicates a retention of cellular elements in the presence of escaping fluid The red cell hematocrit becomes concentrated as the shock develops The specific gravity of the plasma decreases The concentration of the circulating total protein uniformly falls, and there is a marked decrease in the total circulating protein The circulation time increases as the arterial and venous pressures decline The fluid which exudes from the traumatized bowel is serosanguineous and has a protein content varying between 3 and 4 grams per 100 cubic centimeters

Dogs have been studied without anesthesia, with nembutal anesthesia alone, and with

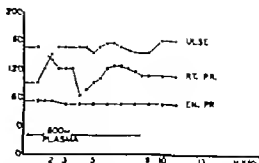


Graph 2. Therapeutic effect of whole plasma. Dog 40-80.

anesthesia plus trauma. The blood and plasma volumes, the hematocrits, and the protein determinations are tabulated in Table II. The first two groups represent the average percentage changes in groups of experiments; the results in the shock group are tabulated individually. The most striking change noted in the shock group is the very marked fall in the circulating protein which varied from 33 to 66 per cent of the original content. These results correspond to the decrease in the plasma volume but are accentuated by the fall in the concentration of the circulating protein. The protein concentration has never increased in this type of shock. Nembutal anesthesia produces a dilution of the hematocrit in the normal dog due in part to stagnation of red cells in the spleen. The hemoconcentration



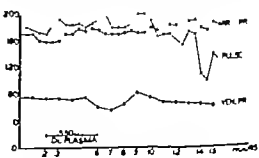
Graph 4. Therapeutic effect of dilute plasma. Dog 40-202.



Graph 3. Prophylactic effect of whole plasma. Dog 40-271.

present in shock is very striking because of the dilution in the control.

Shock treated with whole plasma. The injection of whole plasma in the shocked animal results in a temporary rise of the arterial and venous blood pressure. Dog 40-180 exemplifies the usual reaction to whole plasma (Graph 5). The injection of 250 cubic centimeters of plasma raised the blood pressure from 60 to 110 millimeters mercury. The effect was transitory and the animal died within 2 1/2 hours. The plasma volume was 965 cubic centimeters immediately following the injection and within 2 hours decreased to 500 cubic centimeters. The plasma injection caused a temporary dilution of the hematocrit and a temporary rise in the venous pressure. The prophylactic effect of whole plasma is indicated by the reaction of dog 40-271 (Graph 3). This dog received 800 cubic centimeters of plasma beginning at the time of trauma. In this type of experiment plasma does not prevent the initial fall in blood pressure but tends to stabilize it above



Graph 5. Prophylactic effect of dilute plasma. Dog 40-274.

TABLE III—THE EFFECT ON THE BLOOD VALUES OF HALF DILUTION PLASMA INJECTED THERAPEUTICALLY AND PROPHYLACTICALLY

	Plasma volume c.c.	Hematocrit	Total protein concentration	Total circulating protein gm	
Dog 40-202	805	53.9	6.86	55.0	Control
Therapeutic injection	570	60.8	5.10	29.0	Shock
	950	45.3	5.06	48.0	After plasma
Dog 40-274	570	59.6	5.45	31.1	Control
Prophylactic injection	690	52.7	5.03	34.7	4 hr after trauma
	645	65.7	4.62	20.8	12 hr after trauma

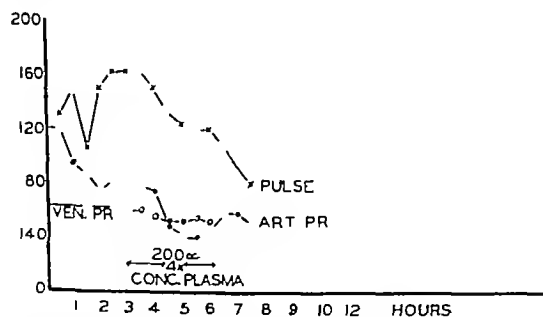
the shock level. At the end of 12 hours the arterial pressure remained at 110 millimeters of mercury, and the venous pressure was within normal limits. The large amount of plasma maintained the plasma volume at a constant level throughout the experiment. The hematocrit did not change during the plasma injection, but gradually increased after the injection.

Shock treated with half dilution plasma Large amounts of dilute plasma will restore the circulation of the shocked dog to an approximately normal condition (Graph 4). Dog 40-202 received 700 cubic centimeters of dilute plasma, the plasma volume was increased to the normal level, and the hematocrit decreased. The blood pressure returned to the control level, and the venous pressure increased to within normal limits.

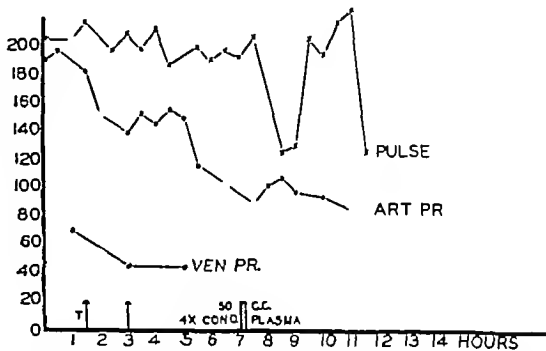
Injection of dilute plasma gives the most uniform response of all the concentrations tested. Dog 40-274 (Graph 5) was given 550 cubic centimeters of half dilution plasma starting immediately after trauma. The arterial and venous pressures, as well as the plasma volume, were maintained at the nor-

mal level for 16 hours. The dog's general condition seemed excellent at the end of this time, but the experiment was terminated by sacrificing the animal. The results in 5 experiments have been similar to that of dog 40-274. Table III illustrates the effect of dilute plasma on the plasma volume, hematocrit, and total circulating protein.

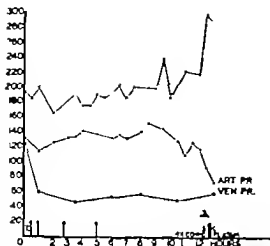
Four times concentrated plasma The effect of injecting a relatively large quantity of the concentrated plasma is illustrated in Graph 6. Dog 40-341 received 200 cubic centimeters with no appreciable effect on the arterial pressure. The venous pressure was fairly well maintained until death. The plasma volume decreased from 774 to 400 cubic centimeters 1 hour before death. In this type of experiment the plasma specific gravity and the plasma protein concentration increase as would be anticipated. The therapeutic effect of the concentrated plasma is apparently variable as an occasional dog did survive longer than dog 40-341. In an occasional experiment of this type, the plasma volume would remain essentially unchanged during the injection, but



Graph 6 Prophylactic effect of concentrated plasma Dog 40-341



Graph 7 Therapeutic effect of concentrated plasma Dog 41-15



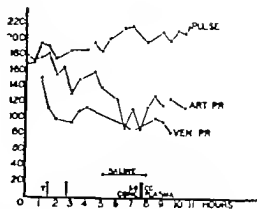
Graph 8 Therapeutic injection of concentrated plasma, 45 cubic centimeters of saline given by stomach tube. Dog 4 6.

in spite of this the blood pressure fell followed by the death of the animal

Four times concentrated plasma has been injected intravenously into an animal with peripheral circulatory failure. If the amount used is comparable to the quantity which has been used in a patient suffering from shock, the effect on the blood pressure, venous pressure, and on the dog's general condition is negligible. Repeated experiments (6) have produced the same negative result, as demonstrated in Graph 7.

The use of four times concentrated plasma does not supply available water to replenish the depleted circulating plasma volume. Graph 8 represents an experiment in which the dog was given water by stomach tube when the blood pressure was 70 millimeters of mercury. The concentrated plasma was then injected intravenously but the circulation was not improved. It must be admitted that in this type of shock the absorptive surface of the bowel has been damaged by trauma, hence this may not be a fair trial of the oral administration of water supplemented by concentrated plasma.

The type of experiment in which concentrated plasma seemed to have a beneficial effect on the blood pressure is shown in Graph 9. The dog was given saline solution by subcutaneous injection when the blood pressure was falling. When the pressure had reached 70



Graph 9 Therapeutic injection of concentrated plasma, 40 cubic centimeters of saline injected subcutaneously. Dog 4 9.

concentrated plasma was injected. This was followed by a temporary improvement in the circulation.

ANALYSIS OF RESULTS

The type of peripheral circulatory failure produced by peritoneal trauma conforms essentially with that produced by the usual experimental methods. This is characterized by a fall in the arterial and venous pressures, a decrease in the plasma volume and a concentration of the hematocrit. The plasma protein concentration uniformly decreases. This is not in agreement with the more generally accepted concept of protein concentration, but does agree with the observations of Dunphy who found a decreased concentration in experimental burnshock. The most striking feature is the very marked decrease in the total circulating protein which raises the intriguing problem of determining its fate. A considerable amount can be recovered in the peritoneal exudate but at the present time it is not possible to state the proportion lost by this route. The data suggest that there is also a general loss of protein throughout the body but the experimental evidence is not conclusive. This will be discussed in a future publication.

The results indicate that dilute plasma is more efficient than concentrated plasma in the prophylactic or therapeutic management of experimental peripheral circulatory failure. The intravenous injection of large volumes of

one-half dilution plasma have prevented the development of shock. Whole plasma has a similar effect. The results obtained with the concentrated plasma are at best unpredictable, and are not comparable to those obtained with either of the other forms.

The fluid which is lost from the bowel contains 3 to 4 per cent protein, and it seems logical that both fluid and protein should be replaced in the same proportion. Theoretically, the injection of four times concentrated plasma might increase the plasma volume by withdrawing fluid from the tissue spaces. This assumes that such fluid is readily available. The results of these experiments indicate that with the peripheral circulatory failure of shock this extravascular fluid cannot be reclaimed in effective amounts by the use of hypertonic solutions. Fluid must be made available by parenteral injection or concentrated plasma injections will only add to the already increased viscosity of the blood. The increased efficiency of the concentrated plasma supplemented by a saline hyperdermoclysis supports this contention.

It should be emphasized that it is extremely hazardous to compare experimental results with conditions which occur in clinical practice. The type of shock studied in the laboratory is severe, and very large amounts of plasma are required to be effective. However, large amounts of dilute plasma have been useful in preventing operative traumatic shock (10). The experiments also indicate that very large amounts of plasma may be necessary in treating the patient. This has also been emphasized by Dunphy and others. If the circulating plasma volume of a patient is depleted to 50 per cent of its normal amount, the usual 500 cubic centimeter transfusion would be extremely inadequate in treatment of the profound shock. A logical argument in favor of the concentrated plasma is that clinically one deals with a well hydrated individual who has rapidly developed shock following an injury. Also that the four times concentrated

material might modify the factors leading to circulatory failure until the injury can be adequately treated. This can only be determined by extensive clinical trial.

Experimentally supporting evidence has not been found. It appears unlikely that fluid can be reclaimed by hypertonic plasma after shock has become established.

SUMMARY AND CONCLUSIONS

1. Experimental shock has been produced by intestinal trauma. This type of shock is characterized by a reduction in the circulating plasma volume, a concentration of the hematocrit, a decrease in the plasma protein concentration and specific gravity, and a marked decrease in total circulating protein.

2. The therapeutic and prophylactic value of half dilution plasma, whole plasma, and four times concentrated plasma in treating experimental shock has been compared.

3. Large amounts of half dilution or whole plasma are more efficient than concentrated plasma in this type of shock.

4. The large amount of protein lost from the circulation has been emphasized.

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THE ENDOCRINE ASPECTS OF CHRONIC MASTITIS

Further Report on Rates of Estrogen Excretion and Results of Hormone Therapy

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FROM a wealth of clinical observation and laboratory experiment, it is now known that the proliferation and atrophy of the epithelial and certain of the connective tissues of the breast depend upon the rise and fall in the function of several endocrine glands. The internal secretions of the ovary are in fact, essential for the very existence of the mammary gland as an active organ. Since breast tissue is clearly a prerequisite for the development of chronic mastitis, the hormones which maintain the breast in this state are also necessary factors. Regarding this point there can no longer be any disagreement. Yet, in spite of much discussion of chronic mastitis as an endocrine disease, no one has yet succeeded in proving that this breast condition represents a specific response to any recognized type of glandular dysfunction.

The first step toward the solution of the problem of chronic mastitis is the establishment of what constitutes the essential tissue change taking place in the breast. In particular it is necessary to consider if chronic mastitis is not actually a collection of several diseases each with a distinctive morphology and each with a special set of causative factors.

CLASSIFICATION OF CHRONIC MASTITIS

Most classifications of chronic mastitis have been based on small histological sections from surgical specimens in which rather localized processes, such as cysts or papillomas, attain an exaggerated importance. In considering this disease from a functional standpoint, however it is necessary to regard the breast

as a whole and to base a classification on clinical characteristics, on the gross examination of tissue or on the study of histological sections taken outside of areas of circumscribed neoplastic activity.

From our study based on such criteria, it has appeared that there are easily distinguishable two major types of breast reaction to what might prove to be endocrine agents. (a) In the first type there may be only premenstrual pain and swelling, but usually there develops also a tender nodular induration of the outer quadrants. Gross section of such breasts reveals a dense shining white fibrous tissue. (b) In the second type there is a milky or oily secretion from the nipple with perhaps some palpable dilatation of the large ducts beneath the areola. Section reveals dilated tubules of all sizes from which may be squeezed a grayish white or brown fluid material. In previous studies efforts have been made to determine the histological basis of these two clinical types (66) and the nature of the surgical lesions arising in them (69).

TYPE 1: The histological changes in the breast in which there is only pain and premenstrual swelling are difficult to evaluate because of a dearth of surgical material from such cases. In a few sections studied there appeared to be only a loosening of the periacinar connective tissue suggestive of an increase in interstitial fluid in that area (Fig. 1). This appearance has been described as a premenstrual edema of the periacinar connective tissues and referred to by several writers. The condition of simple premenstrual pain and swelling seems however to pass directly into the next stage in which clinically detectable changes in breast structure are present.

In the breast with diffuse outer quadrant induration the most striking histological

From the Memorial Hospital Breast Service of Dr. Frank E. Wood.

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change was found to be a connective tissue proliferation, which distorted the gland fields, compressing and scattering the small ducts and acini (Fig 2) In many cases, however, it appeared that there was also a proliferation of acini, giving a morphologic structure resembling adenomyosis of the uterus (Fig 3) As an accurate description of the process in the breast and to bring the terminology into harmony with that used in the pelvis, the term *adenofibrosis* for this variety of chronic mastitis seems most fitting Semb in his exhaustive pathological study of chronic mastitis adopted the term "fibroadenomatosis" indicating a conception of morphology of the disease very similar to the one here presented

TYPE 2 In the breast with secretion from the nipple (Fig 4) there was found dilatation of the ducts with amorphous material and desquamated cells in their lumens Periductal edema with collections of lymphocytes was a common finding, but diffuse fibrosis was absent The pathological process in this condition evidently takes place in quite different components of the breast structure from that in adenofibrosis and leads to correspondingly different morphologic results Clinically this condition may be called nonpuerperal lactation or galactorrhea, but in its pathological aspects it appears as duct dilatation with stasis of secretions

With both types of breast disease the areas selected for surgical excision contain, as might be expected, more complicated types of epithelial hyperplasia (Figs 5 and 6) These no doubt constitute the practical therapeutic problems, but it has been the concentration of attention on these localized, but perhaps only secondary, manifestations of epithelial activity that has caused some neglect of the generalized breast changes that might permit the study of some constitutionally effective etiologic agent

POSSIBLE FACTORS IN THE ETIOLOGY OF CHRONIC MASTITIS

Before the enumeration of the endocrine aspects of these two types of chronic mastitis it will be useful to consider two hypotheses which are, at least for the moment, tenable in regard to their cause

1 According to a currently popular view, the cause of chronic mastitis is an excessive, prolonged, or unbalanced endocrine stimulus acting principally on the epithelium Hyperplasia of the ducts and acini of the breast could, for example, be expected to result from stimulation by the estrogens, abnormal secretion, from an anterior pituitary hormone or the sudden withdrawal of an ovarian hormone If this concept were correct, chronic mastitis would be the actual equivalent of conditions produced in the laboratory by the injection of various endocrine substances

2 The breast is, however, also subject to effects produced through disturbances in its nervous and vascular systems The rapidity with which the premenstrual swelling of the breast develops each month can indeed only be explained on the basis of a vascular reaction with an increase in the fluid content of the mammary tissues Such a fluid increase may be due to the ovarian hormones, which are known to cause a general fluid retention (70) as well as a concentration of fluid in certain portions of the reproductive tract (4, 5, 78) Vascular change may also be initiated through the nervous system, as shown in recent experiments on the mammary blood volume of cattle (59) and in reported examples of sudden increase in the size of the human breast after psychic stimuli (67)

That permanent organic change in breast structure may be the result of an alteration in the chemical environment of the cells, caused by local vascular disturbances, is an easy hypothesis to offer, but difficult to prove Chronic congestion has, however, been held the cause of pathological effects in various parts of the body, but particularly in the organs of reproduction In the female it has been held responsible for the sclerotic and cystic ovary (33), for adenomyosis of the uterus (48) and for the so-called chronic parametritis (28), in the male for prostatic hypertrophy (41) Adenofibrosis is a disease arising in a related organ with morphologic features very similar to those of adenomyosis and prostatic hypertrophy

At least two theories must therefore be considered for the etiology of chronic mastitis The first asserts that the condition is the

result of abnormal stimulation of the breast, particularly of the epithellum by one of the ovarian hormones. The second view suggests that as a result of nervous and perhaps endocrine stimuli the breast becomes the seat of chronic or repeated vascular congestions, producing conditions that lead eventually to a fibrosis or an adenofibrosis in which later secondary epithelial changes of all sorts may develop. The evidence for these two conflicting views will be taken up under five principal headings.

CLINICAL CHARACTERISTICS OF CHRONIC MASTITIS

The symptoms and signs of the two types of chronic mastitis give the clinician at once some indication of the nature of the conditions.

The pain and swelling which are such important aspects of the *adenofibrosis* type have been ascribed by some writers to the premenstrual proliferation of breast epithellum (35) and by others to the dilatation of the ducts with desquamated cells (14). Actually, there is little morphologic evidence either for a cyclical proliferation or cyclical desquamation of human breast epithellum. It seems almost certain, on the other hand that the premenstrual tension of the breast with its associated tenderness is due to a regularly recurring vascular engorgement or increase in interstitial fluids. Pain on this basis would of course be increased when fibrosis of the breast is present and the premenstrual swelling of the susceptible periacinal tissues must take place within a relatively unyielding fibrotic stroma. If an analogy is to be made with the symptoms of any pelvic condition, it must be with the congestive type of dysmenorrhea, with its characteristically premenstrual discomfort or perhaps with adenomyosis and endometriosis. None of these is now regarded as essentially an endocrine disease.

Secretion from the nipple is, however a symptom which points in a rather different direction. The source of some nipple discharge is undoubtedly local as in the instance of serous fluid coming from a duct containing a papilloma. In cases in which there is a milky

secretion from many ducts of both breasts or a discharge of semisolid, fatty material, the functional response of the breast to its natural, endocrine stimulus is closely imitated. Here then an endocrine cause seems likely from the clinical findings.

COMPARISON OF THE HISTOLOGY OF CHRONIC MASTITIS WITH BREAST CHANGES EXPERIMENTALLY PRODUCED BY HORMONES

The second point concerns the many attempts to reproduce the disease in animals by the administration of endocrine substances. With the injection of various hormones, especially the estrogens, pathological proliferation of the epithelial elements in the mammary gland certainly occurs (9 29). Some workers have insisted on the similarity, if not identity of these induced tissue changes with those of the spontaneously developing chronic mastitis of women (11 35 36 37 38). This question of course strikes at the root of the problem because if the laboratory lesions are the same as those found in human chronic mastitis, the cause of the latter disease is already known. If they are different, new factors or an entirely new hypothesis must be sought.

A systematic attempt to compare the histology of chronic mastitis with the lesions artificially produced in animals by hormone administration was recently made at the Memorial Hospital (69). Sections from 102 cases of human chronic mastitis were first studied and the lesions tabulated. For comparison the mammary glands of 163 mice that had been treated with one of four different hormone substances were examined. The essential change produced in the mice by estrogen administration was a proliferation of new acini. There was slight epithelial hyperplasia of the duct lining and sometimes dilatation of ducts with desquamation of cells and stasis of secretion. Fibrosis though reported to occur after hormone administration (2 16) was a most insignificant feature in our series of animals.

From this study it was concluded that the essential changes of adenofibrosis, which takes place to a large extent in the interstitial tissues, are not identical with those produced in the laboratory by hormone injections (Fig. 7).

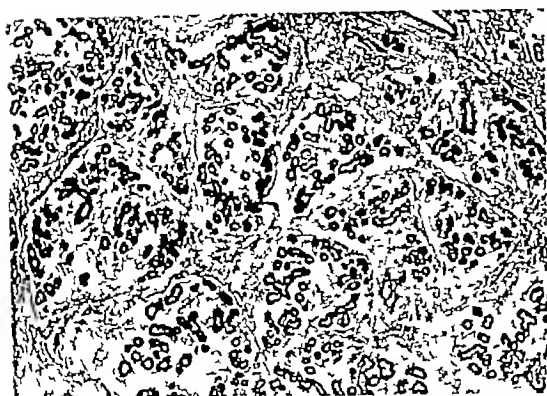


Fig 1 Intralobular "edema" of the periacinar connective tissue



Fig 2 Adenofibrosis of the breast with fibrosis as the predominant process



Fig 3 Adenofibrosis of the breast (left) and, right, adenomyosis of uterus in contrast

On the other hand, effects somewhat comparable to those found in women with dilated ducts and a non puerperal secretion are producible by these means (Fig 8)

NATURE OF THE ASSOCIATED DISORDERS FOUND ELSEWHERE IN THE REPRODUCTIVE TRACT

Gynecologic investigation of the patient with chronic mastitis must yield facts of considerable significance, for it is almost certain that any constitutional agent capable of affecting the breast must have its effect on the uterus also. Thus a glandular disorder

producing chronic mastitis should cause at least disturbances of menstruation and fertility. On the other hand, were a chronic congestion resulting from nervous or hormone factors prominent in the breast disease, signs of a similar condition might also be expected in the pelvis. From previous articles reporting the gynecologic status of patients with chronic mastitis, four aspects may be selected to stress again (65, 67, 69)

The menstrual history Disturbances of menstruation certainly affect a minority of women with chronic mastitis. A decrease in



Fig 4. Abnormal secretion with duct dilatation



Fig 6. Localized duct hyperplasia in case with abnormal secretion.

the amount or duration of the menstrual flow in women with painful breasts has however previously been described by at least 7 clinicians (69). From a total of 261 patients derived from two series of published cases (67, 69) it is also our opinion that this anomaly of menstruation is significantly more frequent in patients with the engorgement fibrosis syndrome (adenofibrosis) than in normal women of the same age groups (Table I). The significance of the scant menstruation in these cases is not clear. Beyond the simple fact of the short flow there is little reason to suppose a primary underfunction of the ovary. It is at least as likely that processes taking place in the interstitial tissues of the breast are re-

peated in the pelvis to cause a local interference with the blood supply in the uterus with a locally conditioned diminution in flow.

One point at least in regard to the uterine function of these patients is quite clear. Their endometrial patterns give no indication of any excessive hormone stimulation (67). Perhaps the most popular endocrine hypothesis offered to explain chronic mastitis is that of an excessive estrogenic and a deficient corpus luteum activity. The effects of this type of disturbance on the uterus have long been recognized as a cystic hyperplasia of the endometrium usually associated with a metrorrhagia. Yet patients with chronic mastitis are not especially susceptible to this disease nor do gynecologic patients with endometrial hyperplasia show any tendency to the development of breast disorders of this type.

In some contrast to the patients with adenofibrosis there is among the women with nonpuerperal secretion a high incidence of prolonged menstrual intervals or amenorrhea (Table II). This may in theory be interpreted as the result of a persistent corpus luteum or perhaps of periods of depressed ovarian function during which excessive anterior pituitary activity is released.

Reproductive and lactation histories. In our group of cases about a half of all patients with the adenofibrosis type of chronic mastitis have had no children (Table III) while over 80 per cent of those with nonpuerperal secretion have had full term pregnancies. On the basis of this now fairly considerable series it appear



Fig 5. Localized adenomatous proliferation in case of adenofibrosis

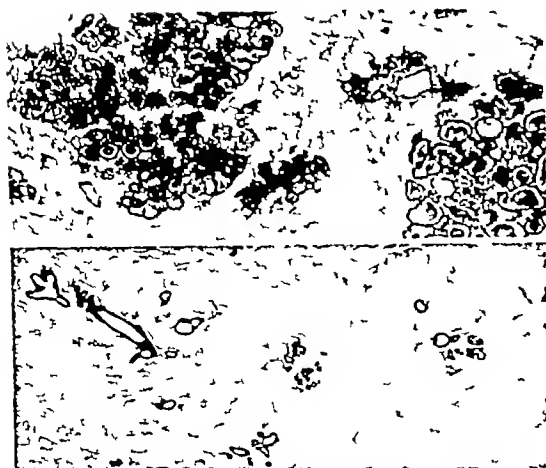


Fig 7 Estrogen produced acinar hyperplasia of mice above, in contrast with spontaneous adenofibrosis of women, below



Fig 8 Estrogen produced duct disease in mice, above, in contrast with dilated ducts containing secretion in women, below

that adenofibrosis is definitely more common in the unmarried and in those who, though married, have not conceived. The question is open as to whether the failure to bear children led to the chronic mastitis or the conditions associated with the disease predisposed to the relative sterility.

The pathology of the ovary in cases of chronic mastitis. Many of the hyperplastic or neoplastic conditions occurring in the female reproductive tract have been associated by some observer with "cystic ovaries," and among these chronic mastitis is no exception. The functional significance of such ovaries is, however, not known. In one group at least the ovary with small cysts may be quite fibrotic with a reduced rather than an increased function (33). Nothing in the appearance of the ovaries observed during gynecologic operation in women with adenofibrosis of the breast suggests a hyperfunctioning organ (67).

Organic lesions in the pelvis. The cause of breast lesions has frequently been attributed

to organic lesions in the pelvis. The most far reaching claims for this viewpoint were made by a former president of the American College of Surgeons, Dr C. Jeff Miller, who reported the cure of breast conditions following operations for fibroids, for retroversion, and for adnexal disease. Our experience has not been as satisfactory. Of 24 patients with chronic mastitis in whom gynecologic therapy for coincident pelvic lesions was carried out, 8 were apparently cured of their breast disease (65). Since this is about the proportion in whom spontaneous cures or remissions may be expected, it is improbable that such miscellaneous pelvic lesions can be held responsible for breast disease.

Nevertheless, it remains probable, unless chronic mastitis is due to purely local factors, that some equivalent process should be found taking place in the pelvic organs of reproduction. On the basis of a large series of gynecologic examinations it has appeared to us that such an

TABLE I—DURATION OF MENSTRUAL BLEEDING IN TWO TYPES OF CHRONIC MASTITIS

	Adenofibrosis	Abnormal secretion
Total No. cases	261	93
Normal periods, per cent	75.1	64.5
Short periods, per cent	16.8	17.2
Long periods, per cent	3.8	4.3
Amenorrhea, per cent	4.2	7.5
Menopause, per cent	0	6.4

TABLE II—MENSTRUAL CYCLE IN TWO TYPES OF CHRONIC MASTITIS

	Adenofibrosis	Abnormal secretion
Total No. cases	261	93
Normal cycle, per cent	71.3	44.1
Long or irregular cycle, per cent	13.8	25.8
Short cycle, per cent	9.9	14.0
Amenorrhea, per cent	4.2	7.5
Menopause, per cent	0	6.4
Others, per cent	0.8	2.1



Fig. 4. Abnormal secretion with duct dilatation.



Fig. 6. Localized duct hyperplasia in case with abnormal secretion.

the amount or duration of the menstrual flow in women with painful breasts has however previously been described by at least 7 clinicians (69). From a total of 261 patients derived from two series of published cases (67, 69) it is also our opinion that this anomaly of menstruation is significantly more frequent in patients with the engorgement-fibrosis syndrome (adenofibrosis) than in normal women of the same age groups (Table I). The significance of the scant menstruation in these cases is not clear. Beyond the simple fact of the short flow there is little reason to suppose a primary underfunction of the ovary. It is at least as likely that processes taking place in the interstitial tissues of the breast are re-

peated in the pelvis to cause a local interference with the blood supply in the uterus with a locally conditioned diminution in flow.

One point at least in regard to the uterine function of these patients is quite clear. Their endometrial patterns give no indication of any excessive hormone stimulation (67). Perhaps the most popular endocrine hypothesis offered to explain chronic mastitis is that of an excessive estrogenic and a deficient corpus luteum activity. The effects of this type of disturbance on the uterus have long been recognized as a cystic hyperplasia of the endometrium, usually associated with a metrorrhagia. Yet patients with chronic mastitis are not especially susceptible to this disease nor do gynecologic patients with endometrial hyperplasia show any tendency to the development of breast disorders of this type.

In some contrast to the patients with adenofibrosis, there is among the women with nonpuerperal secretion a high incidence of prolonged menstrual intervals or amenorrhea (Table II). This may in theory be interpreted as the result of a persistent corpus luteum or perhaps of periods of depressed ovarian function during which excessive anterior pituitary activity is released.

Reproductive and lactation histories. In our group of cases about a half of all patients with the adenofibrosis type of chronic mastitis have had no children (Table III) while over 80 per cent of those with nonpuerperal secretion have had full term pregnancies. On the basis of this now fairly considerable series it appears



Fig. 5. Localized adenomatous proliferation in case of adenofibrosis.



Fig 7 Estrogen produced acinar hyperplasia of mice above, in contrast with spontaneous adenofibrosis of women, below

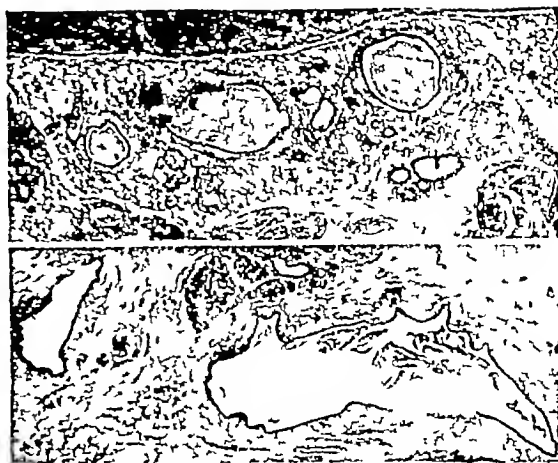


Fig 8 Estrogen produced duct disease in mice, above, in contrast with dilated ducts containing secretion in women, below

that adenofibrosis is definitely more common in the unmarried and in those who, though married, have not conceived. The question is open as to whether the failure to bear children led to the chronic mastitis or the conditions associated with the disease predisposed to the relative sterility.

The pathology of the ovary in cases of chronic mastitis. Many of the hyperplastic or neoplastic conditions occurring in the female reproductive tract have been associated by some observer with "cystic ovaries," and among these chronic mastitis is no exception. The functional significance of such ovaries is, however, not known. In one group at least the ovary with small cysts may be quite fibrotic with a reduced rather than an increased function (33). Nothing in the appearance of the ovaries observed during gynecologic operation in women with adenofibrosis of the breast suggests a hyperfunctioning organ (67).

Organic lesions in the pelvis. The cause of breast lesions has frequently been attributed

to organic lesions in the pelvis. The most far reaching claims for this viewpoint were made by a former president of the American College of Surgeons, Dr C. Jeff Miller, who reported the cure of breast conditions following operations for fibroids, for retroversion, and for adnexal disease. Our experience has not been as satisfactory. Of 24 patients with chronic mastitis in whom gynecologic therapy for coincident pelvic lesions was carried out, 8 were apparently cured of their breast disease (65). Since this is about the proportion in whom spontaneous cures or remissions may be expected, it is improbable that such miscellaneous pelvic lesions can be held responsible for breast disease.

Nevertheless, it remains probable, unless chronic mastitis is due to purely local factors, that some equivalent process should be found taking place in the pelvic organs of reproduction. On the basis of a large series of gynecologic examinations it has appeared to us that such an

TABLE I—DURATION OF MENSTRUAL BLEEDING IN TWO TYPES OF CHRONIC MASTITIS

	Adenofibrosis	Abnormal secretion
Total No. cases	261	93
Normal periods, per cent	75.1	64.5
Short periods, per cent	16.8	17.2
Long periods, per cent	3.8	4.3
Amenorrhea, per cent	4.2	7.5
Menopause, per cent	0	6.4

TABLE II—MENSTRUAL CYCLE IN TWO TYPES OF CHRONIC MASTITIS

	Adenofibrosis	Abnormal secretion
Total No. cases	261	93
Normal cycle, per cent	71.3	44.1
Long or irregular cycle, per cent	13.8	25.8
Short cycle, per cent	9.9	14.0
Amenorrhea, per cent	4.2	7.5
Menopause, per cent	0	6.4
Others, per cent	0.8	2.1

TABLE III.—REPRODUCTIVE HISTORY IN TWO TYPES OF CHRONIC MASTITIS

	Atrophic 26	Unusual secretion 93
Total No. cases		
Single, per cent	34	54
Married no pregnancies, per cent	26.7	7.5
Married miscarriages only per cent	3.8	3
Married 1th children, per cent	50	83.8

associated condition does frequently exist. This takes the form of a disease scarcely referred to in the American literature but widely discussed abroad under the name of chronic pelvic congestion (15) or chronic parametritis (26, 27, 28, 40). According to Freund chronic parametritis begins as a vascular engorgement and, if it persists, ends as a general fibrosis of the pelvic supporting structures. It is interesting that in his patients with chronic parametritis Freund described painful breast nodules, while we have found that nearly a third of the patients with the typical engorgement fibrosis syndrome in the breast exhibit the broad ligament tenderness so characteristic of the descriptions of chronic parametritis (Table IV). It is possible furthermore that some of the patients with "cystic ovaries" with supposed salpingo-oophoritis and with severe erosions of the cervix belong in this group. Were they added the clinical incidence of pelvic congestion in women with premenstrual breast symptoms might easily reach 50 per cent. It appears then that a syndrome of which vascular engorgement and fibrosis are prominent features does often occur simultaneously in breast and pelvis.

ASSAYS OF URINE FOR HORMONE EXCRETION

In a previous study the rates of estrogen excretion and blood level figures on 20 women

with various types of benign breast disease were presented (67). No abnormalities were found at that time which could be regarded as characteristic of any group of these cases. At least two records of similar work have been reported since that time. Wanke and Jaulsen studied the cycles of 2 cases of "mastopathia chronica" and found a low estrogen excretion. Opposite conclusions were reached by Bucher and Geschickter who made determinations of the estrogens and pregnandiol in the urine of patients with mastodynia and adenosis and concluded that these cases had a corpus luteum deficiency or a relative hyperestrinism.

Since our report of 1936, 9 further patients have been studied with revised technical procedures. These cases included 3 normal women, 3 with very pronounced pain and engorgement of the breasts and 3 with a bilateral secretion of a milk-like fluid.

Techniques employed in hormone assay. In each case all of the urine excreted during the cycle was collected in 72 hour lots. The original intent had been to determine simultaneously the excretion of total estrogens, of pregnandiol and of gonadotropic substances.

The estrogens were extracted with slight modifications according to the method described by Smith and Smith (6, 61). Hydrolysis as carried out first by boiling for 4 hours a 500 cubic centimeter specimen with 4 cubic centimeters of concentrated hydrochloric acid. The urine was then extracted for 48 hours with benzol and the extract represented a concentration of hundred times assayed on castrated white mice. For this purpose 6 spayed mice primed 8 days previously were used for each injection level. A reaction was accepted as positive only when of these animals showed fully cornified smears.

end point one was
t 5 gamma / 16 35

TABLE IV.—FREQUENCY OF GYNECOLOGIC

to publish the results on the 80 measurements of pregnandiol that were made. With this reservation it may be stated, however, that no abnormal trends in pregnandiol excretion were evident in the group of menstruating women with chronic mastitis.

Description of results in the 9 subjects studied
Although this work was based on the study of only 9 subjects, the following histories of the 6 with chronic mastitis show that they were in each instance extreme examples of the types of disorder they were selected to represent. Changes in total estrogen excretion, if any exist for these conditions, should have been apparent in such a group.

CASES 1, 2, and 3. These were young, unmarried women without breast or pelvic disease. The menses were normal except that during the study of 1 case, an unexpected delay was encountered. The estrogenic hormone excretion in these cases for the month amounted to 3500, 4600, and 4000 mouse units, respectively. Gonadotropic substance was detected in measurable amounts at the time of ovulation in 2 of these cases.

CASE 4. R. E., admitted September 18, 1937, was a married woman of 29 years with a history of a single pregnancy, ending in a 4½ month miscarriage, 6 months before her admission to the clinic. Menstruation had characteristically been of the 21 to 24 day cycle type with long 7 day periods. Since the miscarriage there had been marked premenstrual breast pain.

The patient remained under observation in the clinic for a year, during which time she continued to complain of severe premenstrual breast symptoms associated with lower abdominal discomfort and backache, dyspareunia, and leucorrhea. A condition of anxiety dependent on home conditions was evident.

Examination of the breasts on several occasions showed them to be medium in size, dependent, very tender with a moderate outer quadrant nodularity. The pelvic examination showed that the fundus was normal in size and position, but with marked tenderness on any manipulation of it. The adnexa and parametria were tender, the cervix hypertrophied with an endocervical discharge.

Hormone assays were carried out, beginning with a menstrual period of June 9, 1938 and ending with the onset of the next period 26 days later. The total excretion of estrogens was 1282 mouse units. No gonadotropic substance was found, but death of the test animals resulted in a failure to get any record of 3 specimens.

CASE 5. J. G., admitted November 11, 1937, was a woman of 28 years, twice married. By a former husband she had had 1 child, now 11 years old, who had been successfully nursed for 7 months. A second marriage of 4 years' duration had been infertile, although no contraceptives were used. Men-

strual periods had always been normal, occurring every 28 days and lasting 6 days. A suspension of the uterus had been performed 3 years before admission.

The present illness, having its onset 8 months previously, consisted in a bilateral premenstrual pain and swelling of both breasts beginning 7 to 14 days before each period. Examination showed the breasts to be medium in size, tender with moderate nodularity of the left one and marked induration of the right. Pelvic examination showed the fundus to be normal, a little tender on motion, the adnexa, normal, the cervix, moderately eroded. During the patient's year of observation in the clinic she developed backache, premenstrual pelvic pain, dyspareunia and dysuria. Cystoscopic examination showed only a trigonitis and the urine was sterile.

Hormone assays were begun with the period of April 8, 1938, and continued for 35 days of the cycle. The total excretion of estrogens was 6030 mouse units. Gonadotropic substance was present during 2 three day specimens of the cycle, but these unexpectedly were the days immediately after the menstrual bleeding.

CASE 6. H. J., admitted December 11, 1937, was an unmarried girl of 24 years, whose periods had always occurred at 35 day intervals and been so scant as to be described by her as "negligible." There had always been moderate pelvic dysmenorrhea, but for 7 years there had been in addition very severe pain and swelling in both breasts for 2 weeks before each menstrual period.

Examination showed a rather slender girl with large breasts, diffusely thickened throughout and markedly dense and nodular in the outer quadrants. The breasts were also very tender. No pelvic examination was ever done.

Hormone assays were carried out during the cycle beginning on March 13, 1938. The total excretion of estrogens was 5085 mouse units. Gonadotropic substance was present in the specimen representing the fifteenth, sixteenth, and seventeenth days before the following period.

The patient was later treated with progesterone before her periods receiving 3 units during one month and 15 units the next. Before a subsequent period she received 150,000 units of estradiol benzoate, without affecting the breast symptoms or the amount of menstrual flow.

CASE 7. B. S., admitted January 23, 1937, was a married woman of 38 years, the mother of 2 children, ages 7 and 12. They were each nursed only 1 month on account of painful nipples. The menstrual periods formerly occurring every 28 days and lasting 4 days had stopped abruptly and without apparent cause 3 years before admission. Since that time there had been slight spotting on 3 occasions, but none during the previous year. Flushes had never developed.

For 7 years there had been a discharge from each nipple. Eight weeks before admission there had been a sudden swelling and hardness of the left

TABLE V--TOTAL ESTROGEN EXCRETION IN NORMAL WOMEN AND IN WOMEN WITH CHRONIC MASTITIS

[illegible][illegible]

breast associated with fever. These acute symptoms had subsided but lumps had persisted in the lower part of the left breast.

Examination showed that the breasts are large and pendulous with nodular areas about both areolae. Pressure over the areolae produced milk discharge from several ducts on both sides. Pelvic examination showed no abnormalities and no evidence of trophoblast.

The patient was observed for over a year with little or no change in the breast condition. Operations for the lumps were considered on several occasions but these tended to disappear. On May 9, 1938 hormone assays were begun and continued for 30 days. The excretion of estrogens during this time was 366 mmoles units, a low figure but no gonadotropic substance was demonstrable.

CASE 8. M G admitted January 15, 1938 as married woman of 38 with 3 children, aged 7 and 10 years. Lactation had been discontinued after months of each child owing to deficient secretion of milk. Menstrual periods had always been normal, occurring every 8 days and lasting 5 days. One abortion 7 years ago had been followed by removal of the left tube and ovary.

The present illness began 3 weeks before admission with sudden enlargement and the appearance of milk in both breasts. There had been no irregularity of the menses.

Examination showed the breasts large and peduncles somewhat tender and definitely nodular. Pressure over the areolae produced a profuse milky discharge and some thick casts of ducts. The pelvic examination was entirely normal.

Beginning with the menstrual period of January 3, 1958, hormone assays were continued for 26 days. The total estrogen excretion was 3683 mouse units and no gonadotrophic substance was detected. This rate of estrogenic excretion was clearly in the normal range.

CASE 9 H. G. admitted 11 v 3, 937 married woman of 3 years had had child 3 years before and no other pregnancies. For years before admission (January 7 933) she had had gynecologic operation with removal of both tubes and the left ovary for salpingitis isthmica nodosa of the denomyosis type and small benign papillary cystadenoma of the ovary. A second operation 6 months before admission (October 23 936) resulted in the removal of the uterus and the remaining ovary for multiple follicle cysts. Menstruation before the first operation had been normal, occurring every 5 days and lasting 7 days and as average amount. After the first operation it became irregular (12 intervals of 6 to 8 weeks and duration of only 36 days. After the second operation all menstruation ceased.

From the time of her only pregnancy there had been constant secretion of little fluid from both nipples but this increased abruptly after the second operation. Also there appeared at that time some pain and considerable swelling of the breast.

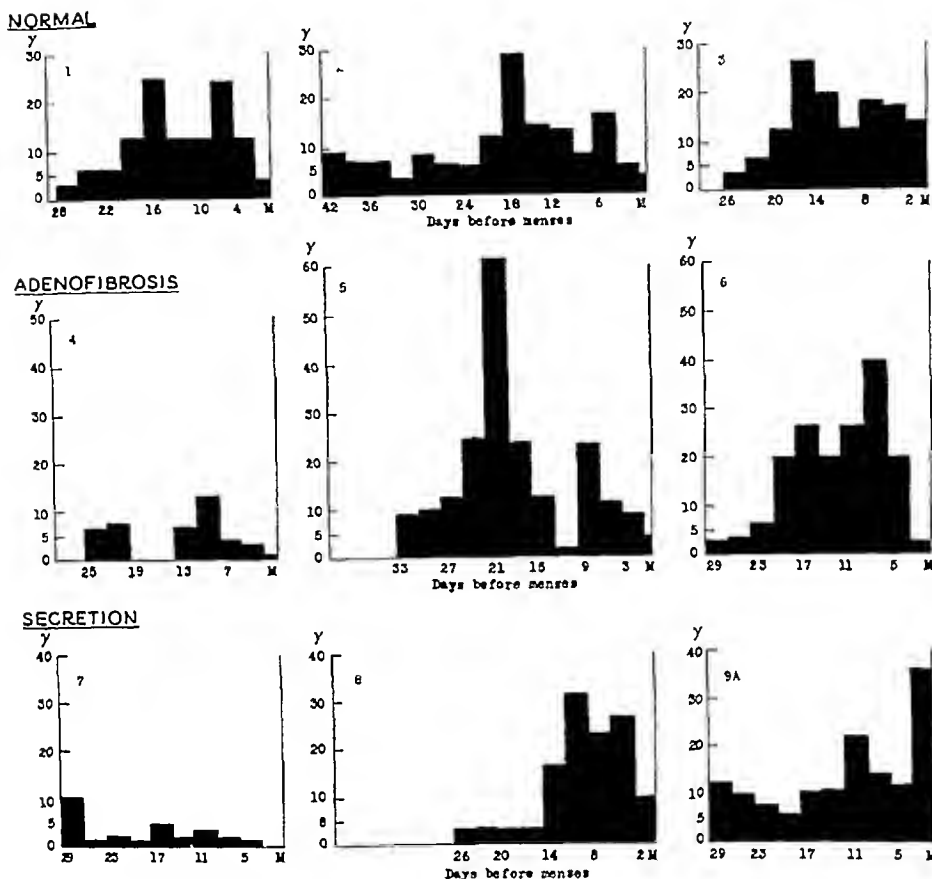


Chart 1 Total estrogen excretion in normal women and in chronic mastitis

Examination on May 3, 1937, showed the breasts to be medium in size, soft and dependent. From each breast large quantities of milk could be expressed in thin streams. Pelvic examination showed no masses in the pelvis and little evidence of atrophy. The sella turcica was later found by x ray on July 18, 1938, to be "very small and the posterior sphenoidal process thin."

Four complete sets of hormone determinations were made on this patient (Chart 2). (a) The first, carried out from March 3, 1937, to April 28, 1937, yielded 4,284 units of estrogen. Gonadotropic determinations based only on the microscopic examination of the ovaries gave 1 positive reaction. (b) Beginning May 3, 1937, the patient received 4,000 international units of amniotin 3 times a week for a month. The breasts were unaffected. Determinations of urinary estrogen from May 16 to June 16, 1937, during the period of administration suggested an actual fall in excretion. This month's urine was extracted in duplicate by 2 separate methods using benzol in the Smith and Smith extractor and ethylene dichloride in a simple stirring

apparatus. The figures for the two methods were 2,177 and 1,751 respectively. (c) Beginning on June 18, 1937, the patient received 3 injections weekly of 50,000 units of estradiol benzoate for a total of 600,000 units. Estrogen excretion rose to 17,318 units for the 30 days of this study. During this month the breasts were somewhat more swollen and tender than previously, but no diminution in secretion occurred. (d) For a few months after these injections there was little improvement and the patient complained rather bitterly of the breast pain. Then improvement set in. A further set of estrogen determinations made after 14 months and during this period of improvement showed the month's excretion to be 4,074 units, a figure almost identical with that obtained in the first month of study when the abnormal milk secretion was at a maximum.

Summary of results of hormone assays The results obtained in each of the 115 bio-assays for estrogenic hormone have been tabulated (Table V) and are shown in Chart 1. The specimens in which gonadotropic substance

were found in the urine are also indicated in the table

Certain points need to be stressed

The monthly excretion of estrogens for the 3 normal subjects ranged from 3,500 to 4,600 mouse units. Gonadotropic hormone was detectable in 2 of these women at the middle of the cycle. The normal estrogen figures are distinctly higher than those previously reported by us, the difference apparently being due to the additional step of acid hydrolysis. The close agreement of the figures for the 3 normal women is probably accidental and it would be unsafe to consider as abnormal any excretion rate within the range of 1,500 to 6,000 mouse units a month.

The first 2 of the 3 cases of adenofibrosis were married women with symptoms to be regarded as due to an associated pelvic congestion. In each the breast symptoms were of short duration, but in each changes in the texture of the breasts were present. Both women had normal menstrual cycles, and 1 had recently been pregnant. The estrogenic hormone excretion of the 2 showed a wide difference, 1,200 to 6,000 mouse units, in a single cycle. One showed gonadotropic excretion near the time of the menstrual cycle.

The third patient was of a different type being a single girl who had had scant menses and severe breast pain and swelling since the onset of her periods. No symptoms suggestive of associated pelvic congestion were present. The structural breast changes, almost certainly predominantly fibrosis, were very pronounced. The estrogen excretion was 5,085 mouse units, a high figure, but probably within the normal range. Gonadotropic hormone at the mid point in this cycle might be interpreted as evidence of a normal pituitary stimulus to ovulation.

The 3 cases of abnormal secretion illustrate the extraordinary variety of clinical and hormone conditions under which this symptom may appear. All were in married women who had borne children but 1 patient was menstruating normally (Case 8). 1 had ceased spontaneously at the age of 35 (Case 7) while 1 (Case 9) had recently undergone a surgical operation with the removal of her uterus and supposedly all of her ovarian tissue. The

monthly estrogen excretion in these cases was 900 units, 3,600 units and 4,300 units, respectively. In none of these were excessive quantities of gonadotropic hormone detectable in the urine.

The third case (Chart 2) deserves special comment for three reasons. (1) The figure of 4,300 units of estrogen excretion is a most unexpected finding in a woman who had apparently suffered the surgical removal of both ovaries. (2) When estradiol benzoate to the amount of 600,000 units was given, the total estrogen excretion in the urine was significantly raised but no alteration in breast symptoms occurred. (3) When 14 months later the abnormal breast secretion had begun to diminish total estrogen excretion in the urine was at the same level as that noted when the breast symptoms were at their height. There appeared then to be no correlation between abnormal lactation and estrogen excretion or administration in this extensively studied case.

In judging the significance of these results the general value of urinary assays as a measure of endocrine function needs to be considered. It should be remembered first that when an estrogenic substance is injected intramuscularly as little as 2 to 3 per cent is recoverable in the urine. There is no reason to suppose that the several thousand mouse units of endogenous hormone which appears in the urine during a month a cycle represents any larger fraction of the total amount being produced by that individual. When contrasts of the ovarian function of different subjects are made on the basis of their urinary estrogen the assumption is evidently being made that the excretion rates have a pretty constant ratio to rates of hormone production. There is, however, little justification for assuming that this is true. The possibility that the proportion of effective estrogen, which is excreted may vary greatly in different individuals, taken with the large error inherent in the technical methods requires that very large differences in urinary estrogen be present before differences in ovarian function may be claimed. Similar comments must be made about the gonadotropic hormones whose study in the urine of nonpregnant women has been

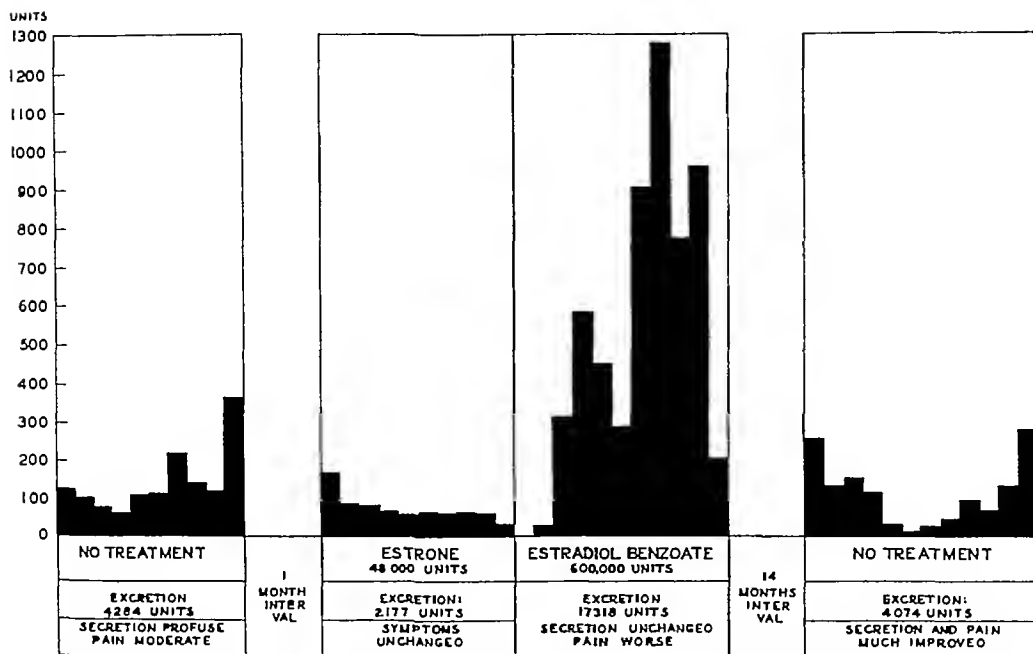


Chart 2 Relationship of estrogen administration to rates of hormone excretion and to symptoms in a case of chronic mastitis

given considerably less trial than has the estimation of the estrogens. The significance of the absence of the hormone at the time of ovulation or its appearance on unexpected days of the cycle is unknown.

The results show then that in patients with the adenofibrosis type of chronic mastitis a wide range may be found in total monthly estrogen excretion, that the average figure is close to that for normal women, that the extremes are probably within the normal range and that typical peaks of estrogen excretion occur. In 1 case at least gonadotropic hormone appeared in the urine at the expected time for ovulation. Women with breast engorgement and adenofibrosis do not therefore display any characteristic disturbance of ovarian or anterior pituitary function, as determinable by these methods.

In the cases with abnormal secretion from the breast a wide range in the figures for monthly estrogen excretions was present. There was also room for the claim in 2 of the 3 cases that the contour of the excretion curves was abnormal in the sense of an absence of pronounced peaks in estrogen excretion.

The failure of large quantities of gonadotropic substance to appear in the urine of the 2 amenorrheic women of the group is of possible interest. Some peculiarities in hormone excretion are therefore present, as might be expected with such pronounced disturbances of menstruation. One cannot, however, on the basis of these studies be precise as to the nature of the hormone disorder in cases of abnormal breast secretion.

THE HORMONE THERAPY OF CHRONIC CYSTIC MASTITIS

The results of endocrine therapy in chronic mastitis is pertinent to the subject, since proof of the effectiveness of such an agent would be strong evidence for the hormone nature of the disease. A review of the history of hormone therapy in breast conditions is a disillusioning exercise.

Chronic mastitis has been treated by each of the new sex endocrines as they became available and, to judge from published reports, all methods have been more or less successful. Substances which have allegedly been followed by improvement include the following ova-

TABLE X.—RESULTS OF HORMONE THERAPY IN RELATION TO FREQUENCY OF SPONTANEOUS IMPROVEMENT

Type of treatment	Total cases	Pain		Nodularity		Secretion	
		Cases with the symptom	Per cent cured or improved	Cases with the symptom	Per cent cured or improved	Cases with the symptom	Per cent cured or improved
Hormone therapy			78				
Observation only	30	26	87	25	83		
All hormones immediate results		64		64			
All hormones results after years	66	64	97	64	97	1	15

patients about three-quarters reported improvement or cure following their supposed treatment.

The explanation of these somewhat surprising results is simple enough. The pain and premenstrual engorgement are symptoms varying in a given woman from month to month. The patient with this type of breast disease almost invariably applies to a physician in great anxiety at a time of exacerbation of symptoms. It is almost a certainty that from the peak of symptoms which brought the patient to the clinic some amelioration will occur in immediately succeeding months.

It has been our experience, however, that when fibrotic change has developed in the breast to any marked degree although it may become less painful or even symptom free some evidence of nodularity will persist almost indefinitely. The secretion of milky or oily material from the nipples is also a condition subject only to gradual change. It lasts as a rule for many months and even well into the menopause.

Effect of injections of various hormones in chronic mastitis. Between 1932 and 1939, 73 cases of chronic mastitis have been treated in the Memorial Hospital Breast Clinic by injections of some hormone preparation. The

Although many of these patients were treated some time ago acknowledgment should be made to Dr. Max Gilbert of the Schering Corporation for estradiol benzoate (progynon B) and testosterone propionate (andron) to Dr. J. C. Marshall of E. R. Squibb and Sons for supplies of estrone (menomet) gonadotropic hormone (menotropin) and prolactin.

TABLE XI.—HYPOTHETICAL SCHEME OF RELATIONSHIP OF TYPES IN CHRONIC MASTITIS

	Type of endocrinosis	Type of ductal disease
Stage of functional disturbance	Premenstrual engorgement, Mastodynia	Postmenstrual secretion, Galactorrhoea
Stage of diffuse tissue changes	Nodular induration of outer quadrants, Fibrosis, Mastectomials	Duct dilatation, Stasis of secretion, Periductal inflammation
Stage of localized secondary symptoms		Typhoid becoming indistinguishable
	Adenomatous proliferation of the small ducts and acini, Cysts	Hypertrophy of ducts, Papillomas, Cysts
Causative factor	Ovarian hormone, Nervous factor, Vascular factor	Ovarian dysfunction, Endocrine dysfunction

substances employed included the following: various preparations of estrogens, in doses ranging from less than 3,000 to more than 100,000 international units a month; estradiol benzoate in doses up to 600,000 units a month; lactogenic substance (prolactin); gonadotropic luteinizing substance; corpus luteum and testosterone propionate. The distribution of cases, the dosage employed, and the effects of the therapy both during and after treatment are given in detail in Tables VII, VIII, and IX.

From a study of Table VIII it appears probable that some improvement in the pain of adenofibrosis occurred during the actual months of administration of testosterone propionate and perhaps also of prolactin. Re-evaluation of the cases after 2 years, however, showed that in no hormone group was the improvement in the pain or nodularity significantly greater than in the control series (Tables IX and X). There was indeed a possibility that the estrogens actually retarded recovery since the proportion of improved cases in the groups so treated was actually lower than could have been anticipated from spontaneous remission alone.

In regard to the symptom of abnormal secretion one must note that the figures point to an improvement in one-third of the hormone-treated cases, 2 years after therapy was given. On the other hand evidence for an immediate effect was slight, a point em-

phasized by the failure of 600,000 units of estradiol benzoate to suppress the secretion in Case 9

Effect of radiation of the ovaries In contrast to the results obtained when stimulating hormones are employed, are those obtained when the ovaries are removed or radiated. The cases, in which such therapy for breast disease is justifiable, are of course exceptional. Our experience with 18 cases so treated (68) show that pain is invariably cured or improved and the nodularity usually somewhat lessened. Abnormal secretion, on the other hand, is very slightly affected for some time.

Summary on Therapy From this experience it is our opinion that glandular therapy up to the present time has been of no benefit in the treatment of chronic mastitis. No hormone we have used to date has produced permanent results exceeding the anticipated rate of spontaneous improvement. The estrogens in particular are probably contraindicated in view of their capacity to cause epithelial proliferation and breast engorgement. The androgens and perhaps progesterone may produce temporary improvement by suppressing ovarian function, but there is no reason to suppose that these results will be permanent. The single established fact in regard to hormone therapy is that abolition of the ovarian function by castration will cause cessation of pain in almost all cases of adenofibrosis and a slow but definite disappearance of the nodularity.

SUMMARY AND CONCLUSIONS

In Table XI is presented a scheme of the relationship of different types of so-called chronic mastitis. It is presented as a hypothesis which seems best to explain the facts now available on this subject.

There are two types of abnormal reaction in the breast which appear to be the result of hormonal or other constitutional agents. Each appears in a purely functional stage, but on the basis of each characteristic organic changes may develop.

Type 1 (adenofibrosis) is at first characterized only by premenstrual pain and swelling, which seems almost certainly to be due to vascular engorgement or increase in tissue fluids. A diffuse induration of the outer

quadrant of the breast due to a proliferation of the connective and epithelial tissues is, however, found in most of these cases and indicates a second stage. A relationship between the excessive premenstrual engorgement and the development of the diffuse fibrosis is suggested by the almost invariable association of the two conditions. Isolated nodules of epithelial activity produce the lumps that require excision but are perhaps purely secondary, localized phenomena developing on the basis of the general adenofibrosis.

Among causative factors it is evident that an actively functioning ovary is a prerequisite to the development of this disease. Yet the infrequency of changes in the cycle of menstruation, the usually normal endometrium, the inability of various workers to agree on any abnormality of hormone excretion and the apparent failure of all endocrine therapy (except castration) speak against any simple quantitative abnormality of sex hormone physiology.

The clinical evidence for an excessive premenstrual vascular reaction in the breasts of these patients is unmistakable and with this are often found clinical signs of a similar disorder in the pelvis. A general nervous instability often with local hyperesthesia of the breast is commonly present in these patients. Many signs point therefore to the need of studying these nervous and vascular factors to determine whether through such agents an abnormal environment may be set up about cells of the breast which could lead to the organic changes of adenofibrosis.

Type 2 (nonpuerperal secretion) in its functional stage is characterized by a milky discharge from the nipple and histologically perhaps by slight hyperplasia of the acini. There soon develops a condition in which dilated ducts become filled with desquamated cells and stagnating secretion. That periductal inflammation, cysts, and hyperplastic or metaplastic changes in the duct lining may result when such a condition is of long standing seems probable.

In many cases of this type an endocrine disturbance in the form of grossly disturbed menstrual cycles is quite evident. Atypical curves

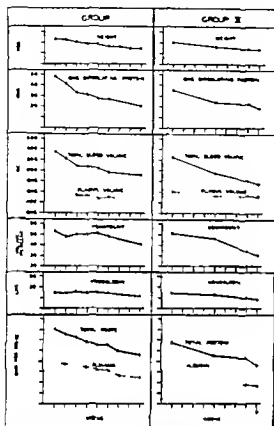


Chart 1. A series of changes in weight, total circulating protein, total blood and plasma volume, erythrocyte volume per cent (hematocrit), hemoglobin, total serum protein and albumin fraction concentration in groups of 4 dogs each during 8 weeks on low protein diet.

Changes in blood volume after intervals of 30 to 40 minutes were calculated from variations in the erythrocyte volume per cent. Hematocrit determinations were made on heparinized blood with the Winthrobe tube.

Serum protein determinations were made by the micro-Kjeldahl procedure. Albumin and globulin were separated by the use of 25 per cent sodium sulphate. Nonprotein nitrogen determinations were made according to the Kock McMeekin method (7) modified for reading with the photoelectric colorimeter (9). All determinations were made in duplicate.

Blood for plasma transfusions, withdrawn from a group of donor dogs, was prevented from clotting by the use of heparin except in

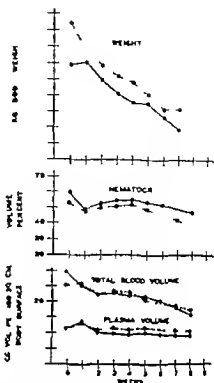


Chart 2. Change in weight and erythrocyte volume per cent (hematocrit) and total blood and plasma volume per unit of body surface in each of dogs during 8 weeks of protein depletion.

one instance when sodium citrate was used. Plasma, removed by centrifugation and stored in liter flasks at 0 degree to 4 degrees C. until ready for transfusion was analyzed for total protein, albumin and globulin concentration. The total serum protein concentration of the pooled donor plasma varied from 5.6 to 6.3 grams per cent.

RESULTS

Effect of low protein diet on blood volume and serum proteins. In order to study the changes in the weight, total circulating protein, total blood volume, plasma volume, hematocrit, hemoglobin, and both the total and the albumin fraction of the protein concentration after the inauguration of the protein free diet, a group of 4 dogs (group I) was studied at weekly intervals until there was a marked hypoproteinemia. The results are shown in

Chart 1 from which it is noted that there is a gradual decrease in all the values over a period of 8 weeks. It is apparent that the decrease in the total protein concentration is due to the diminishing albumin fraction.

To eliminate excessive bleeding as a factor in the development of hypoproteinemia another group of 4 dogs (group II) also shown in Chart 1 was studied at monthly intervals. It was found that the development of hypoproteinemia and changes in blood volume were similar to those seen in group I. In 2 dogs (Chart 2) total blood and plasma volumes were calculated on the basis of 100 square centimeters of body surface area (5). The plasma volume decreased slightly with the development of hypoproteinemia and reduction in the absolute plasma volume. By these same methods of calculation the total blood volume decreased proportionately with the development of anemia and a decrease in the absolute plasma volume.

Effect of plasma transfusions on blood volume and blood proteins in hypoproteinemic dogs. Two hypoproteinemic male dogs were given volumes of plasma calculated theoretically to restore the serum protein level to a normal value of 7 grams per cent. The plasma was injected into the jugular vein with a syringe and the entire amount was given in about 10 minutes. These animals were continued on the low protein diet during the period of observation which lasted a week.

The most striking effects (Chart 3) were the immediate but transient increases in the total blood and plasma volumes, both returning to the pretransfusion levels within 5 days. The injected plasma exerted a diluting effect as shown by the hematocrit values. The protein concentration and total circulating protein of the sera showed only a comparatively small rise despite the large amounts of plasma injected.

A study of the serum proteins and blood volumes after small daily transfusions of plasma for 2 weeks was made in 5 hypoproteinemic dogs (Chart 4). Analyses were made at intervals of 18 to 24 hours after the preceding transfusion.

A single daily 50 cubic centimeter transfusion of plasma was followed by a gradual

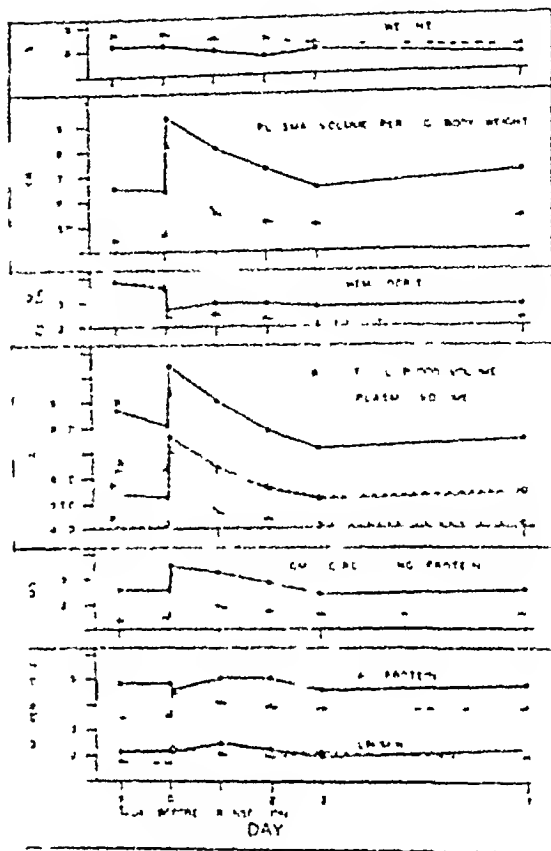


Chart 3. Immediate and late effects of massive plasma transfusion upon plasma volume per kilogram of body weight, hematocrit, total blood and plasma volume, total circulating protein, total serum protein and albumin fraction concentration in two hypoproteinemic dogs. — No. 1, given 220 cubic centimeters of plasma. TP = 5.37, A/G = 1.05. — No. 2, given 215 cubic centimeters of plasma. TP = 6.16, A/G = 1.44.

increase in the serum protein concentration in 3 dogs. At the end of the experimental period there were increases of 20, 23, and 58 per cent above the initial hypoproteinemic level. The effect of removal of about 120 cubic centimeters of blood in each animal for analyses during the 2 weeks period cannot be adequately gauged. It would seem that without this withdrawal the actual increase in protein concentrations might have been appreciably greater. The absolute plasma volume showed no change in 2 animals and increased 12 per cent in 1 dog at the end of the experiment. From the percentage concentration of serum proteins and the plasma volumes, it was pos-

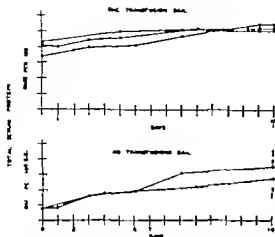


Chart 4. Effect of one or two small (50 c.c.) plasma transfusions daily upon the serum protein concentration of 5 hypoproteinemc dogs.

sible to calculate the total circulating protein these values were 22, 40 and 60 per cent respectively above the pretransfusion levels.

Two hypoproteinemc dogs (Chart 4) were transfused twice daily with 50 cubic centimeters of plasma. The increases in serum protein concentration were 57 and 75 per cent above the initial values. The absolute plasma volumes of these 2 dogs increased 15 and 25 per cent, respectively. The calculation for the total circulating protein showed that there was an increase of 91 and 137 per cent, respectively in these animals. The total blood volumes in these 2 groups of animals decreased during the period of experimentation due to the increasing anemia. Plasma volume per unit of body surface increased slightly with the rise in serum protein concentration in both groups of dogs (Chart 5).

EVALUATION OF STUDY

The changes occurring in serum protein in 5 dogs maintained on a protein free diet are similar to those previously reported by Weech and his co-workers. These investigators described a gradual decrease in the plasma albumin and an accompanying increase in plasma globulin. In the present experiments, it was found that the albumin fraction decreased but that there was no consistency in the behavior of the globulin fraction in the

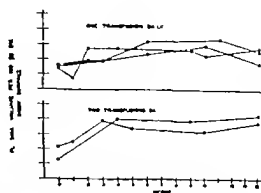


Chart 5. Effect of one or two small (50 c.c.) plasma transfusions upon plasma volume per unit of body surface area.

individual experimental animals. The decrease in the albumin globulin ratios was due to the decrease in the albumin concentration rather than to the increase in globulin concentration.

A number of investigators (4, 14, 17) have associated a decrease of the plasma albumin concentration with a proportionate drop in plasma volume. There was no attempt made by these authors to determine the effect of weight loss by correlating plasma volume changes per unit of body weight or body surface. In the present experiments the plasma volume showed only a slight reduction per unit of surface area despite the loss of weight and the decrease in plasma albumin.

Weech demonstrated that the protein concentration of a hypoproteinemc dog could not be returned to normal by a single massive transfusion of plasma. His work has been confirmed in these experiments. In addition accurate determinations indicated that the blood volumes in these animals were only temporarily increased after transfusions of comparatively large amounts of plasma. From the work of other investigators (3, 19, 27) it appears that plasma proteins can be utilized or stored in animals that have undergone protein depletion. Hence it is not surprising that transfused plasma given in single large amounts did not appreciably increase the serum protein concentration in hypoproteinemc dogs.

Daily single plasma transfusion in small amounts was responsible for a moderate in-

crease in the serum protein concentration of hypoproteinemic dogs. More frequent transfusions (twice daily) produced a marked increase in the protein concentration. Despite the rather marked increases in serum protein concentration, changes in plasma volume, both absolute and per unit of body surface were relatively slight.

SUMMARY AND CONCLUSIONS

1 The protein concentration, total blood volume, and plasma volume were determined in dogs made hypoproteinemic by feeding an essentially protein-free diet. There was an appreciable decrease in the blood protein and volume on such a diet. Plasma volumes calculated on the basis of body surface area also decreased during the depletion period.

2 Single plasma transfusions, calculated to restore the serum protein concentration of these hypoproteinemic dogs to normal, were ineffective.

3 Serum protein concentration was effectively increased by small plasma transfusions given once or twice daily.

4 There appeared to be a relationship between serum protein concentration and plasma volume, both absolute and per unit of body surface area.

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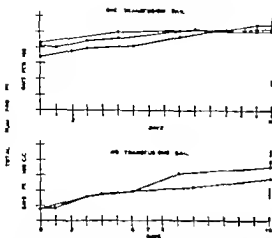


Chart 4. Effect of one or two small (50 cc) plasma transfusions daily upon the serum protein concentration of 5 hypoproteinemic dogs.

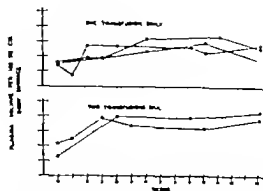


Chart 5. Effect of one or two small (50 cc) plasma transfusions upon plasma volume per unit of body surface area.

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Two hypoproteinemic dogs (Chart 4) were transfused twice daily with 50 cubic centimeters of plasma. The increases in serum protein concentration were 57 and 75 per cent above the initial values. The absolute plasma volumes of these 2 dogs increased 15 and 25 per cent, respectively. The calculation for the total circulating protein showed that there was an increase of 91 and 137 per cent, respectively in these animals. The total blood volumes in these 2 groups of animals decreased during the period of experimentation due to the increasing anemia. Plasma volume per unit of body surface increased slightly with the rise in serum protein concentration in both groups of dogs (Chart 5).

EVALUATION OF STUDY

The changes occurring in serum protein in 8 dogs maintained on a protein free diet are similar to those previously reported by Weech and his co-workers. These investigators described a gradual decrease in the plasma albumin and an accompanying increase in plasma globulin. In the present experiments, it was found that the albumin fraction decreased but that there was no consistency in the behavior of the globulin fraction in the

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Daily single plasma transfusion in small amounts was responsible for a moderate in-

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SUMMARY AND CONCLUSIONS

1. The protein concentration, total blood volume, and plasma volume were determined in dogs made hypoproteinemic by feeding an essentially protein-free diet. There was an appreciable decrease in the blood protein and volume on such a diet. Plasma volumes calculated on the basis of body surface area also decreased during the depletion period.

2. Single plasma transfusions, calculated to restore the serum protein concentration of these hypoproteinemic dogs to normal, were ineffective.

3. Serum protein concentration was effectively increased by small plasma transfusions given once or twice daily.

4. There appeared to be a relationship between serum protein concentration and plasma volume, both absolute and per unit of body surface area.

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AN EVALUATION OF BLOOD AND BLOOD SUBSTITUTES

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WARS have served as the incentive for many advances in surgery. The uses of blood and substitutes for blood have received particular attention in wartime and a number of important contributions have resulted. The employment of stored or preserved blood and of plasma was recommended during the last world conflict, but the suggestions did not receive the attention which they merited. These remarks are not meant to imply that the need for blood and its substitutes is peculiar to warfare. The increase in the numbers of operations and of injuries in civil life has extended greatly the indications for the employment of intravenous injections in the prevention and treatment of peripheral circulatory failure. The realization that shock should be recognized and treated in the early rather than in the fully developed stage has resulted in the saving of many lives.

The importance of the subject under consideration is demonstrated by the fact that one of the first of the studies which were requested of the National Research Council by the Medical Corps of the Army and Navy was on the use of blood and blood substitutes. At the initial meeting of this committee more than a year ago Dr. W. B. Cannon mentioned the need for improvements in methods for preparing, preserving and administering solutions which are already available. In addition, he pointed out the desirability of preparing fractions of blood from man and animals which might be as good as or superior to these fluids. The brilliant work of Dr. Edwin Cohn and his group has resulted already in the separation of human albumen which for some purposes appears to offer many advantages.

In any choice of a blood substitute one must have clearly in mind the particular function of the blood which requires reinforcement. These functions, all interrelated, may

be separated for purposes of discussion. They include oxygen transport by the red cells, osmotic pressure maintenance by the plasma proteins, coagulation through the prothrombin-fibrinogen mechanism, nutrition with special reference to the rôle of the plasma proteins, participation in body response to infection through complement and circulating antibodies, and phagocytosis by the leucocytes.

It is at once obvious that whole blood, and preferably fresh whole blood, is the one fluid which will fortify the circulating blood in the performance of all of its functions. While we shall discuss the relative advantages of given substitutes in various conditions it must be remembered that in most conditions all substitutes for whole fresh blood are inferior. It is doubtful whether under any but a few special circumstances any of the substitutes is superior to whole blood. Even in the hemoconcentration associated with severe burns the objection to the use of whole blood has probably received more emphasis than it deserves. If the total blood volume is maintained at an essentially normal level pronounced degrees of hemoconcentration are tolerated remarkably well.

While in a given instance replacement of blood because of disturbance of a single function is the primary concern several of the functions are probably simultaneously affected. In addition, when dealing with wounded men or with patients on the operating table one must realize that treatment is being given to a person who will not be restored at once to full health. Problems of nutrition, hydration, and infection will have to be met, and the handicapped organism, especially with the additional burdens imposed by wartime conditions, may have difficulty in replacing water, proteins, and perhaps even the formed elements of the blood. Any foreign substance such as acacia or pectin, however valuable its immediate effect must either be excreted with more or less rapidity

in which case its specific effect is temporary and it serves not at all as a real replacement for the depleted stores of protein and circulating cells or else it is deposited in the tissues, where it may be positively harmful. Nevertheless, numerous practical considerations force us to be satisfied with substitutes for whole fresh blood, and for many purposes some of these substitutes are so efficacious that the loss is not great. Thus, almost all of us now use refrigerated blood because of its convenience and availability, reserving the use of fresh unstored blood for special conditions.

In the evaluation of blood substitutes the qualities for consideration are first of all effectiveness and safety. Regardless of all else, our substitute must do its job well without adding unwarranted hazards. Ease and cost of preparation in adequate quantity, simplicity of administration, and capability of storage and transportation are the secondary qualities which determine the choice of a substitute from among those of equal value and innocuousness.

Oxygen transport. Whole human blood is the most effective agent for the transport of oxygen. Blood—fresh, briefly stored, or preserved with added glucose—is the only material available for clinical use which will adequately subserve this function. The older the blood, the fewer are the red blood corpuscles which are intact and the shorter is their expected life in the blood stream of the recipient. Although in stored blood there is little change in this direction during the first week. Preservation of blood with added glucose lengthens the life of the cells and retards the increase in fragility, but has the disadvantages of dilution and large bulk. In shock, when inefficiency of the circulation due to lowered plasma volume interferes with the oxygen-carrying power of the blood, the administration of serum plasma, or any other materials, thereby correcting this condition, at least temporarily results in improved oxygen transport. All of us have seen patients getting along remarkably well with a red blood cell count of 1,000,000 as a result of gradual blood loss. The plasma volume in such cases will be about normal. In acute severe hemorrhage, how-

ever, most patients will not tolerate the loss of even one-half of the total blood volume unless replacement therapy is employed. In other words, although one-half of the red blood corpuscles may still be present in the vascular bed the patient may yet succumb because of the lowered plasma volume. On the other hand, the early administration of plasma or serum following severe blood loss will render more effective the reduced number of corpuscles remaining and recovery will usually result if the bleeding has been controlled. In such circumstances plasma or serum is not so efficacious as whole blood, but the results are usually satisfactory.

In anemia, then, acute or chronic, whole blood, as fresh as possible, is best. In acute hemorrhage any effective blood substitute may be used while whole blood is being obtained or while hemorrhage is being arrested. To treat a patient with a ruptured ectopic pregnancy or a bleeding gunshot or stab wound with plasma or serum alone is to run unnecessarily the risk of increased hemorrhage due to a rise in blood pressure before bleeding is promptly controlled. If the hemorrhage can be safely treated with plasma or serum unless preparations for operation are under way. Even after the hemorrhage has been controlled the resultant severe anemia will handicap the patient and necessitate blood transfusion. When blood is available it is much better to give it at once. And it can now be made constantly available in all hospitals at least.

Recently Amberson in Baltimore, Conn. and in New York, and O Shughnessy in England have aroused interest in the use of hemoglobin alone. Pure crystalline human hemoglobin can be prepared and maintained in stable solution or lyophilized if desired. Because of the efficiency of extracorporeal hemoglobin in carrying oxygen, cells can be kept alive 24 to 36 hours on iceline hemoglobin after all of their red blood cells have been removed. In addition this hemoglobin exerts an osmotic effect several times greater than that of the plasma proteins. Human beings have been given large doses of hemoglobin intravenously without ill effect. The employment of hemoglobin

globin is particularly attractive in view of the volume of red blood cells discarded in the preparation of plasma. The injected hemoglobin however soon alters to inactive methemoglobin and in being excreted throws an added burden on the kidneys.

Maintenance of osmotic pressure of the plasma proteins. Shock represents the chief acute condition requiring the reinforcement of this function of the blood. Again except perhaps in burns whole blood is superior to all other substances. It treats the shock as effectively and at the same time provides red blood cells and, if fresh enough, white blood cells and platelets as well. The exigencies of medical practice however and especially of military medical practice have been responsible for the search for suitable substitutes.

Both plasma and serum are approximately equally effective. There is a somewhat greater likelihood of unfavorable reactions when serum is employed. Plasma contains fibrinogen which serum lacks. They are prepared and administered with about equal ease. Plasma is more conveniently employed in connection with blood banks than is serum but serum is more readily run through bacteriological filters, if that is desired. Both are capable of long storage and transportation—liquid frozen, or dried. As to the relative merits of the substances in the various physical states, liquid plasma is most readily administered frozen plasma preserves the various protein elements best and dried plasma is most conveniently transported. Dried plasma requires expensive and elaborate equipment for large scale production. Liquid plasma offers least resistance to bacterial growth frozen plasma must be rapidly thawed in a water bath at 37 degrees C and dried plasma must be regenerated with distilled water suitable for parenteral use. All have the advantage over blood of being capable of long storage and of not requiring matching before administration. In this last respect they are probably safer than blood, although the possibility of bacterial contamination offsets the advantage of freedom from incompatibility reactions. Liquid or frozen plasma seems best suited to civilian use or to military use on a fixed battlefield, as in England at

present. Dried plasma finds its chief employment in shipment to foreign stations and on naval vessels.

Some workers in the field have put forth as an advantage of the dried material the fact that it can be redissolved in a small volume of water producing a hypertonic solution which, when injected into the blood stream, exerts a powerful osmotic pressure drawing fluid from the tissues and reversing the mechanism of shock as it is stated. Unfortunately most patients in shock—and this is particularly true of soldiers wounded on the field of battle and of burned patients—are not only already dehydrated or in need of fluids, but are entering on a period of their illness when water intake will be of great concern so that it would be well not to increase the tissue water debt at the start. However the idea of administering the proteins from a pint of blood in a single 50 cubic centimeter injection is very attractive and offers possibilities for treatment of shock far forward in the battle zone.

It has been found by Dr Cohn and his associates at Harvard that human plasma can be fractionated into its various protein constituents, which, reduced to pure crystalline states may be redissolved, forming stable nonviscid solutions which flow readily through small needles. Albumen the largest fraction, is the one which exerts the greatest osmotic force. Hypertonic solutions of albumen obtained from alcohol fractionation of human plasma have been employed in a small number of cases and seem extremely effective in the treatment of shock. Unlike the substances which will next be discussed the albumen thus injected is utilized by the body. Production is said to be cheaper and simpler than the preparation of dried plasma, but quantity production is similarly limited by the difficulties in the procurement of large quantities of human blood. Bovine albumen, prepared by the same method, solves the problems of quantity and cost but thus far the bovine albumen has not been free from a small fraction of globulin. The occurrence of sensitivity reactions in human beings given this material has been attributed to this fraction. If bovine albumen which in itself seems not antigenic

can be obtained in sufficiently pure form to be safe, a very nearly ideal plasma substitute for military use and for some civilian uses will have been found.

Human fluids other than blood and its derivatives have been employed. While pleural fluid, and even that occurring in a case of chylothorax, has been safely injected intravenously, most attention has been paid to ascitic fluid. Of this fluid it may be said that it is similar to plasma, but contains roughly half as much protein and is therefore half as effective for most conditions. It is obtained cheaply but in very limited quantities, and the source of supply is undependable. Experience with it is still small. Earlier workers reported frequent reactions. More recent work, using citrated ascitic fluid, seems to have decreased the incidence of reactions. The fluid can be dried, but it seems a waste of time to start with so dilute a fluid. If it can be shown to be free from danger of reactions, it may form a useful source of additional stores in hospitals.

Attempts have been made to use whole beef plasma. Wangenstein in Minneapolis and Muether in St. Louis have demonstrated that some patients tolerate large masses of bovine plasma intravenously although with frequent sensitivity reactions. During the first World War Brodin and St. Giron employed horse plasma in 500 cubic centimeter quantities in several instances without untoward results. It seems unlikely, however, that whole plasma from other animals can be made safe for human use, although suitable purified protein fractions are a distinct possibility.

Animal protein substances of other origins have been proposed, the latest being gelatin which is derived from fish bladders. Dried fish bladders, sold commercially to brewers, when suitably treated yield a readily soluble powder. Injected into dogs the solution is effective in the treatment of shock, causes no reactions, and is not antigenic. Its use in human beings has not been reported, and here as with other foreign substances we must know that the material is not antigenic and that preferably the protein is utilisable by the human organism and is not treated as a foreign substance to be excreted.

Substances of plant origin have also been investigated. Acacia, the complex carbohydrate derived from the gum of certain shrubs of the genus *Acacia*, is the chief of these. It was suggested as a blood substitute as far back as 1906 and was first administered to human beings in 1917. It has been proved to be fairly effective in the treatment of shock, but immediate unfavorable reactions have been too frequent and doubt has been thrown on its eventual fate in the body. It is apparently stored in the liver for long periods and impairs the function of the liver in protein formation. It has also been said to combat the treatment of shock by interfering with oxygen absorption by the red blood cells. For these reasons, and because it fails to supply the whole organism with the additional protein usually required in hemorrhage and in traumatic shock, it has not found much favor.

More recently, common citrus fruit pectin, commercially supplied for the making of jellies, has been prepared by Hartmann and his coworkers for use as a plasma substitute. Only 8 clinical instances of its use are reported, and in at least 1 a chill occurred. It is apparently nonantigenic in guinea pigs, rabbits, and dogs. In the dog it is largely excreted in the urine in the first 48 to 72 hours. Like acacia it is a foreign material of no demonstrable value to the body after the effect of the initial injection has disappeared.

Least effective of all for the reinforcement of the oxygen-carrying power of the blood or the osmotic pressure maintenance are the solutions of the crystalloids. Their benefit is purely temporary. In hemorrhage, unless bleeding has been arrested and shock is mild, they may increase blood loss and wash proteins into the tissues as well. We all recall in the recent past, before the ready availability of blood and plasma radically altered the treatment of sudden shock or hemorrhage, the very brief period of benefit from the injection of solutions of glucose or sodium chloride, except in cases of mild shock in which the precipitating factor had been discontinued.

Blood coagulation. The effect on blood coagulation of the various substitutes has not been comparatively studied. Platelets survive in stored blood for 2 to 5 days. Fresh whole

blood or blood refrigerated for a short time probably increases the clotting power of the recipient's blood and this is probably true of plasma as well. It is not likely that any preparations not derived from human blood will have such power.

Nutrition In speaking of the nutritive rôle of the blood we are now concerned chiefly with its protein content. While the proteins of the blood are formed elsewhere than in the blood stream it has been shown that they may be utilized in turn by the body for storage in the tissues. In conditions of chronic hypoproteinemia the administration of whole blood as long as the hemoglobin is low (as it usually is in these conditions) followed by the administration of plasma or serum is fairly efficacious. Since as a rule, low plasma proteins are associated with depleted protein stores in the tissues, great quantities of plasma must be administered intravenously before any effect is reflected in the level of the plasma proteins. In conditions of starvation, as in esophageal or gastric obstruction, some improvement may be achieved, but will be maintained only if normal alimentation is restored. In nephrosis and cirrhosis, although alimentation may be unimpaired, the continuing loss of proteins makes the problem more difficult. Amino acids injected intravenously (Elman) have proved their worth in supplying the body with building stones for the formation of tissue and blood proteins when adequate protein cannot be taken by mouth. Whipple and Madden have produced digests of casein by pepsin which are not split as far as the amino acid stage and which when administered intravenously will maintain

dogs in positive nitrogen balance indefinitely.

Infection We can expect only whole blood plasma, and serum to supply complement and immune bodies. Any blood substitute which supplies utilizable protein will indirectly aid in antibody formation. Human globulin has been purified as has albumen, and could perhaps find some use in this regard. Substances of plant origin are of no immunological value and acacia, by interfering with the regeneration of plasma protein in the liver may be actually harmful.

Phagocytosis Significant numbers of effective leucocytes can be supplied only in fairly fresh blood. Leucocytes decrease 50 per cent in numbers in 24 hours and phagocytic activity of those remaining drops after 72 hours, is slight in 5 days and absent in 7

SUMMARY

It is obvious that the ideal in replacement therapy is the administration of fluid of the same composition as that which has been lost—whole blood for whole blood and plasma for plasma. The employment of whole blood is rarely contraindicated except in instances of extreme hemoconcentration, such as that which may occur following severe burns. Plasma and serum have the advantage, particularly in emergencies, that compatibility tests are not necessary and delay in treatment can be avoided. Preliminary observations indicate that purified human albumen is a safe and effective substitute for plasma. The problem of providing blood substitutes in large quantities will be greatly simplified if nonantigenic fractions of animal plasma proteins can be prepared.

STAPHYLOCOCCUS SEPTICEMIA

Observations Relative to the State of Hydration in the Dog and in Man

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THE therapeutic problem presented by Staphylococcus septicemia remains a pressing one, in spite of the remarkable advances made in recent years through the development of chemotherapy and the widespread adoption of a physiological approach to therapeutics. The controversy which still exists concerning the efficacy of early or late surgical intervention in acute hematogenous osteomyelitis is characteristic of the confusion in this field and an indication of the fundamental nature of the unsolved problems.

Reports of various investigators stressing the importance of adequate fluid balance in the treatment of burns, intestinal obstruction, and various other acute and chronic surgical diseases, suggested the possibility that fluid imbalance in acute infections may be a factor influencing prognosis. Accordingly, an investigation was initiated having as its object the determination of some of the changes occurring in hydration during Staphylococcus septicemia.

No careful observations on hydration in the toxic phase of staphylococcus infections have been reported. A few fragmentary references indirectly bearing on the matter have been gathered. Webb and Korfmacher concluded that acute infections produce comparatively mild or temporary changes in serum proteins, of total protein, a normal or increased globulin and a decreased albumin level. Jones and Eaton in discussing nutritional edema stressed sepsis as one of the important factors in the causation of postoperative edema. Curphey and Orr made the same observation and stated

that edema was most frequently associated with starvation accompanying an acute infection such as peritonitis. Shumen and Jeghers in their discussion of the value of routine blood protein determinations listed fever as one of the causative factors of hypoproteinemia.

The importance of adequate fluid balance has been more adequately stressed in the study of other surgical diseases. The present day conception of normal water exchange, particularly as regards its clinical application in surgery, has been emphasized in the work of Coller and Maddock and their associates (4, 5, 6). They have shown that the daily maintenance requirements of fluids for the healthy adult is about 3500 cubic centimeters and that the need may be greater with increased metabolism or abnormal losses of body fluids. This investigation drew attention to the necessity for maintaining an equilibrium of electrolytes in the blood and pointed out the dangers of inadequate or excessive administration of sodium chloride.

Jones and Eaton (11, 12) first called attention to nutritional edema as a problem of clinical surgery. In 1933 they reported observations in 34 surgical patients, having critically low serum protein levels following surgery, in most of whom edema occurred. Subsequently, they showed experimentally that postoperative edema occurred following procedures frequently used in patients. It was their opinion that the production of edema was dependent chiefly upon nitrogen starvation and other forms of malnutrition in association with such factors as excessive intake of water and sodium chloride, profuse surgical drainage, general effects of sepsis, massive hemorrhage, or renal dysfunction. They produced experimental evidence that water can accumulate to a striking degree in any of the parenchymatous organs as well as

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In the subcutaneous tissues and that all of the body functions may be greatly retarded by such an occurrence. Ravdin and his associates showed a definite relation between intestinal and gastric emptying times and the level of plasma protein. They pointed out that the edema of trauma after gastrointestinal anastomosis may be accentuated by a lowered plasma protein level to such an extent that an obstruction due to a technical defect in the anastomosis is mimicked. They further emphasized the effect of hypoproteinemia in decreasing the proliferation of fibroblasts and in producing a tendency to wound disruption after abdominal operations.

Shumen and Jeghers, in recommending study of the plasma proteins as a routine procedure for every patient, pointed out the importance of hyperproteinemia as well as of hypoproteinemia. They called attention to the value of the plasma protein level as an indication of liver reserve and particularly stressed its importance in hyperthyroidism as a means of anticipating and avoiding post-operative crisis. In routine tests on 370 patients they found that edema was present in 23 per cent of the 81 patients whose plasma protein levels fell below 6.00 grams per cent. Kormacher also emphasized the relation of the plasma protein level to the severity of hyperthyroidism and stated that levels of total protein below 6 grams per cent or of albumin below 3 grams per cent are probably indicative of hepatic damage and are reasons for performing thyroidectomy in stages. In his opinion plasma protein estimations offer a definite prognosis in obstructive jaundice, since extensive liver damage is made evident by marked reversal of the albumin-globulin ratio.

The study of the rapid shifts in fluid balance occurring after extensive burns has brought to light the important rôle played by the plasma proteins in these physiological changes. Elkinton, Wolff and Lee in a study of 5 cases of severe burns, emphasized the information which is available at the present time. After a 25 per cent burn as much as 53 per cent of the total plasma volume may disappear from the circulating blood within 40 minutes, and the loss continues for as long as 40 hours. During

this early period there may be a tremendous concentration of blood. Such fluid imbalance is primarily due to an altered capillary permeability with a shift of fluid and proteins into the tissues rather than an external loss of these substances. The need for water and electrolytes is moderate only since the excess fluid in the tissues should be available when plasma osmotic pressure is restored to a normal level. Administration of excessive amounts of normal saline without plasma protein only increases an edema already present and must be given in dangerously large amounts to have any significant effect upon the plasma volume. For the correction of this situation Elkinton and his associates recommended the frequent intravenous injections of plasma, in amounts varying according to the need, without the administration of excessive amounts of protein free fluids. Scudder (16) recommended the intravenous use of hypertonic saline solution in conjunction with adrenal cortical extract and showed that these agents have a great effect upon plasma volume in the absence of quantitative protein replacement. Throughout the study and treatment of patients with severe burns frequent plasma protein determinations in relation to hematocrit readings are of the utmost value in indicating the proper therapeutic measures.

In 1938 Scudder, Zwemer and Whipple (18) reported a large series of collected cases of acute intestinal obstruction with an analysis of the clinical and pathological data. Twenty-five patients who came under the direct observation of the authors were subjected to an intensive study. On the basis of these observations the authors drew definite conclusions regarding the efficacy of controlled fluid therapy. The next year Scudder, Drew and Sloan (17) reported in detail a case of acute appendicitis complicated by multiple abscesses in which it would appear the patient's life was preserved only because of the direction of treatment by a definite program of fluid control. They emphasized the observation that earlier than blood pressure changes increasing peripheral hemoconcentration foretells impending circulatory collapse and recommended the adoption of a program of careful fluid balance for all severely ill pa-

tients, stressing the efficacy of concentrated saline, adrenal cortical extract, and plasma as therapeutic agents in combatting impending shock. Scudder and his associates indicated that proper fluid control therapy in surgical conditions producing disturbances in physiological fluid balance can be directed after careful study and rational interpretation of information concerning cell volume and plasma protein levels.

EXPERIMENTAL STUDY

The material presented in this report includes data accumulated from a study of experimental *Staphylococcus septicemia* in dogs and data acquired in observations of patients admitted on the surgical services of Charity Hospital in New Orleans with diagnoses of *Staphylococcus septicemia*.

Observations were completed upon 15 dogs divided into two groups of 7 and 8 animals, respectively. Group I was composed of 4 adult dogs and 3 four month old puppies. Group II was composed of a litter of 8 two month old nursing puppies. Throughout the experiments they were given bountiful quantities of pabulum and standard dog foods. In addition, Group II puppies were allowed to nurse. Fluids were unrestricted, but no attempt was made to force feeding or to administer treatment.

During 2 weeks preceding the experiments normal values were established for hematocrit or red blood cell count and plasma proteins. Blood cultures were taken repeatedly before the beginning of the experiments and were found to be negative. The method used for plasma protein determination was the falling drop method of Barbour and Hamilton (1, 2, 3).

A strain of hemolytic *Staphylococcus aureus* recovered from a human case of *Staphylococcus septicemia* was cultured for 18 hours in dextrose beef heart broth. One cubic centimeter of this inoculum was injected into the right femur of each dog in Group I. Before use in Group II the organism was made more virulent by animal passage, and the 18 hour dextrose beef heart broth culture was concentrated by centrifugation until 1 cubic centimeter of the final inoculum contained 30×10^9 bacteria. One cubic centi-

meter of this preparation was injected into the right tibia of each animal in Group II.

Five dogs of Group I survived, but only 1 animal died as a result of the hemolytic *Staphylococcus aureus septicemia*. All the animals of Group II succumbed after intervals varying from 2 to 17 days. Determinations of hematocrit or red blood cell count, plasma proteins, and blood cultures, together with clinical observations, were made at regular intervals for 16 days or until the dogs died. Autopsies were performed on the 10 dogs which succumbed. Cultures were taken of the various parts, and sections were prepared for microscopy. *Staphylococcus septicemia* was produced in all of the animals, but the blood culture colony counts were much higher in the dogs of Group II. Limited osteomyelitis was present in 9 of the autopsied animals. Metastatic abscesses were found three times in the lungs, twice in the liver, and twice in the kidneys. Marked degenerative changes in the liver, kidneys, and heart were constant findings.

In this study of hydration the method employed by Scudder (9, 16, 17, 18) and his associates was used, since the simple determination of cell volume and plasma proteins gives much useful information concerning fluid balance.

It has been shown by Stebbins and Leake that there is a diurnal variation of as much as 0.044 in the specific gravity of dog blood. Barbour and Hamilton (3) ascribed changes of 0.040 in the specific gravity of dog blood to "emotional anhydremia." Variations are known to occur also in the cell volume and red blood cell counts of normal blood. Because of these normal daily variations in individual animals, composite graphs of the data at hand give more representative pictures of the changes in hydration, occurring in the respective groups of animals under the experimental conditions set forth, than do individual records. Accordingly, observations will be made and conclusions drawn largely on the basis of the composite graphs seen in Figures 1, 2, 3, 4.

Group I The hematocrit curve (Fig 1) rose perceptibly in relation to the hyperpyrexia which developed during the first 4 hours after inoculation. Thereafter, there was an uneven

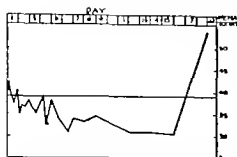


Fig. 2. Group I animals, hematocrit determinations. Average hematocrit curve of 7 dogs during mild *Staphylococcus septicaemia*. The final spectacular rise as caused by single specimen from animal.

but progressive fall in the average hematocrit level until a value of approximately 30 was reached and maintained for several days. The final spectacular rise in the curve was caused by a single specimen from 1 dog. The average plasma protein curve (Fig. 3) starting from a base line of 5.48 grams per cent made a considerable rise on the second day after inoculation and maintained itself irregularly at a level well above the base line. The final rise in the curve was formed here also by a single specimen.

By placing the hematocrit and plasma protein curves in relation to each other one is able to make a reasonable interpretation of the changes which occurred in this particular group of animals. The general picture resembles the idealized graph which Drew Scudder and Pappas (9) thought typical of "water loss with anemia." If it can be assumed that

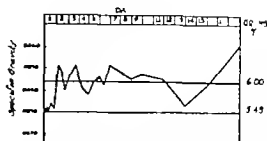


Fig. 3. Group I animals, plasma protein determinations. Average plasma protein curve of 7 dogs during mild *Staphylococcus septicaemia*.

the increased levels of plasma protein were caused by concentration of blood due to water loss the degree of the anemia was in reality greater than that represented.

Group II. The average red blood cell curve (Fig. 4) beginning at a base line of 3,500,000 cells per cubic millimeter fell rapidly and consistently to a level of approximately 2,500,000 cells per cubic millimeter which was reached on the sixth day and was maintained thereafter except for a single specimen from the 1 surviving dehydrated dog on the seventeenth day. The average plasma protein curve (Fig. 4) which rose perceptibly on the second day as did also the curve for Group I was maintained above the base line only until the fourth day. Thereafter there was a sharp decline of the curve to a level below 4 grams per cent. The exceedingly low value of 3.16 grams per cent was reached by a single specimen from the 1 dog surviving on the seventeenth day.

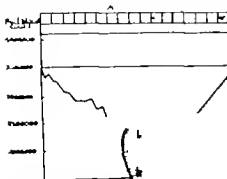


Fig. 4. Group II animals, red blood cell curve of 8 dogs during mild *Staphylococcus septicaemia*. The final single count from animal shortly

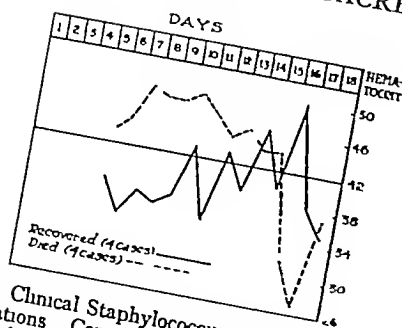


Fig 5 Clinical Staphylococcus septicemia hematocrit determinations Composite graphs of hematocrit determinations during Staphylococcus septicemia in two groups of patients

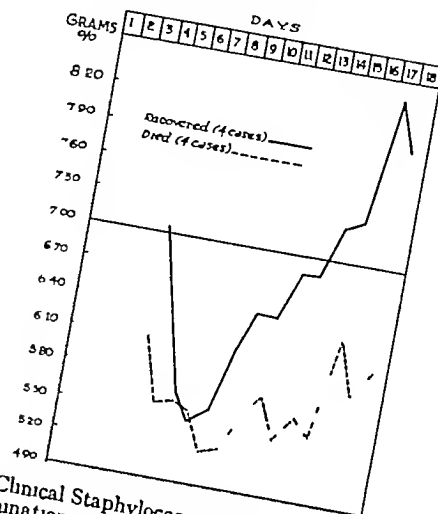


Fig 6 Clinical Staphylococcus septicemia plasma protein determinations Composite graphs of plasma protein determinations during Staphylococcus septicemia in two groups of patients

Again placing the red blood cell curve and the plasma protein curve in relation to each other, one is enabled to make a reasonable interpretation of the variations in fluid balance which occurred. During the first 4 days following inoculation, when there was a steady fall in the hematocrit curve but a moderate increase in plasma protein values, the relation resembled the idealized "water loss with anemia" picture seen in Group I. Between the fourth and fifth days the relation of the respective curves changed to one indicating both red blood cell and plasma protein depletion. If clinical judgment to the effect that the animals were in states of comparative dehydration is correct, the true values for red blood cells and plasma proteins were even lower than those indicated by the curves.

Reasons for the marked decline in the hematocrit curve and the red blood cell curve in the respective groups of animals remain matters for speculation. The actual blood loss incident to the frequent taking of specimens was not great. Since less than 20 cubic centimeters of blood was withdrawn from any animal of Group II in the 25 days during which the observations were made, it does not seem probable that blood so lost figured largely in the more than 28 per cent decline in the red blood cell level. The possibility that there was a depression of the hemopoietic function of the bone marrow is not borne out by the marked erythroid and myeloid activity seen in sections of the bone marrow. Malnutrition may have been a factor, although in each group the greatest decline in the curves

occurred by the sixth day after inoculation, which is a relatively short period for changes from malnutrition to become evident. Staphylococcus hemolysins are capable of rapid destruction of blood, however, microscopy did not reveal any unusual amount of pigment in the reticuloendothelial system, nor was jaundice seen clinically. Loss of hemorrhagic exudates into the intestine and lungs and by external discharges may have been a causative factor in the anemia of 2 of the dogs.

It is easier to suggest reasons for the variance of the plasma protein curves of the two groups, inasmuch as differences in the respective clinical courses were marked. The matter of exudates supplies a ready explanation. Whereas 5 of the animals of Group II produced copious exudates, only 1 dog in Group I lost any considerable amount. However, 2 dogs, which had no marked exudative loss, had lower protein levels than the other animals in Group II.

Destruction of plasma proteins by the direct action of a staphylococcus toxin must remain a hypothetical possibility. Indirect action of such toxins in causing degenerative changes in the liver offers a more likely explanation, if it can be assumed that the advanced state of cloudy swelling and fatty degeneration, observed in all of the histological

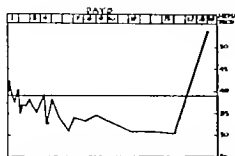


Fig. 1. Group I animals hematocrit determinations. Average hematocrit curve of 7 dogs during mild *Staphylococcus septicaemia*. The final spectacular rise as caused by single specimen from animal.

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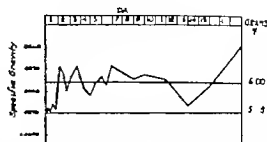


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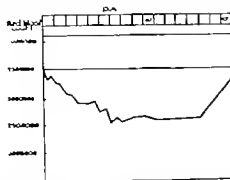


Fig. 3. Group II animals red blood cell count. Average red blood cell curve of 8 puppies during severe *Staphylococcus septicaemia*. The final spectacular rise indicated single count from animal shortly before its death.

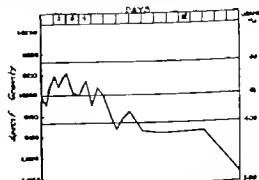


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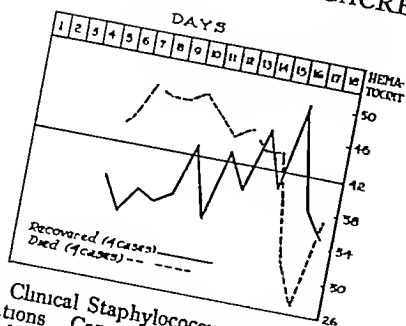


Fig 5 Clinical Staphylococcus septicemia hematocrit determinations Composite graphs of hematocrit determinations during Staphylococcus septicemia in two groups of patients

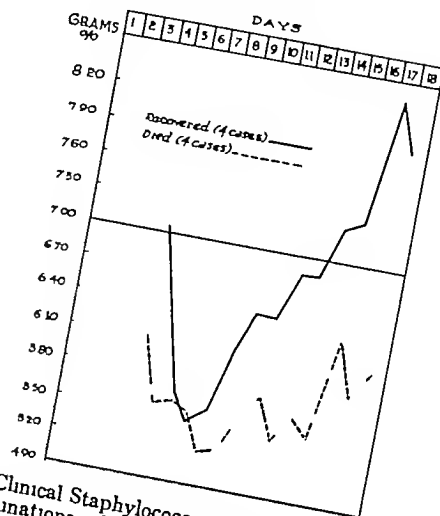


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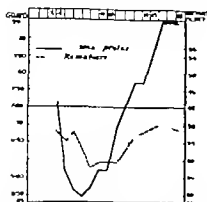


Fig. 7. Graphs of hematocrit and plasma protein determinations during *Staphylococcus septicemia* in boy of 10 who recovered. This patient received 2975 cubic centimeters of blood by transfusion between the fourth and eighteenth days.

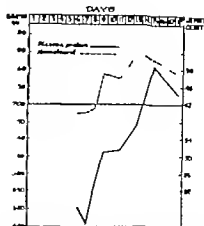


Fig. 8. Graphs of hematocrit and plasma protein determinations during *Staphylococcus septicemia* in girl of 3 who recovered. This patient received 350 cubic centimeters of blood by transfusion between the sixth and thirteenth days.

sections of liver was due, in part, to bacterial toxins. Since the liver is thought to assume an important rôle in the production of proteins the level of the plasma proteins may be an important indicator of liver health. The relation between hypoproteinemia and liver damage in hyperthyroidism and obstructive jaundice has already been mentioned (14). Attention has been directed also, to hepatic changes reported after experimental dehydration (8). Animals in Group II became more dehydrated than those of Group I, and it is probable in view of the procedure used and the clinical course followed by each group that dogs of Group II were exposed, also, to bacterial toxins of greater potency and in greater amounts. It is reasonable to suppose that the degenerative changes observed in sections of liver removed at autopsy were greater than those in the animals which survived and that a lower plasma protein level occurred in Group II partly as a result of more extensive liver degeneration.

Failure to find edema in the face of extremely low plasma protein levels is one of the interesting observations of the study. In 5 animals of Group II plasma protein determinations of less than 3.7 grams per cent were recorded. Jones and Eaton (11) in reporting repeated estimations of less than 3.6 grams per cent in a patient, never subject to edema, suggested that the explanation lay in the ex-

aggerated state of dehydration of their patient. Curphey and Orr and Keefer stated that edema rarely occurs, even in the presence of very low plasma protein, without the administration of the sodium ion, usually as sodium chloride. Explanation of the absence of edema in these experimental animals may be found, therefore in their dehydration and their failure to receive any considerable amount of sodium chloride.

CLINICAL STUDY

Sixteen Charity Hospital patients, each having a clinical diagnosis of *Staphylococcus septicemia*, were observed, and of these 8 were chosen for this report. Repeated blood cultures drawn from each of the 8 patients were positive for the hemolytic *Staphylococcus aureus*. Controlled fluid therapy was employed in each instance, but varied in detail according to the training and diligence of the respective internes and residents. Frequent hematocrit and plasma protein determinations were made in order to furnish data for comparison with those obtained in the study of the experimental animals. Four of the patients survived, whereas the remainder succumbed. In order to correlate the findings in this study with those obtained in the experimental investigation already described, the 8

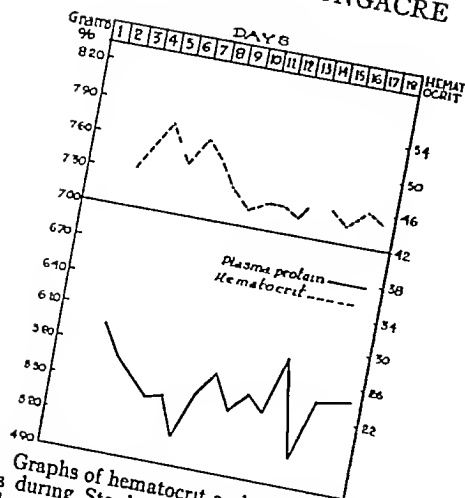


Fig 9 Graphs of hematocrit and plasma protein determinations during Staphylococcus septicemia in a young adult male who died. Blood transfusions were small and comparatively infrequent, 2760 cubic centimeters being given between the third and eighteenth days

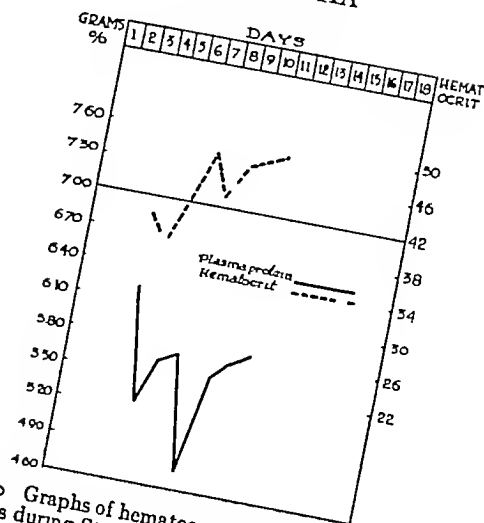


Fig 10 Graphs of hematocrit and plasma protein determinations during Staphylococcus septicemia in a girl of 14 who died in spite of comparatively large amounts of blood by transfusion (3900 cubic centimeters between the fourth and eleventh days). This patient was one who became markedly edematous before death

patients were divided into groups according to survival. Composite graphs of each group's hematocrit and plasma protein readings were made.

Figure 5 shows the composite graph of the hematocrit determinations in each group of patients. It fails to demonstrate the consistent lowering of the hematocrit level which was so striking in both Group I and Group II animals of the experimental study. It would appear that the numerous transfusions which these patients received were sufficient to maintain or raise to comparatively normal levels the hematocrit in those patients who succumbed as well as in those who recovered. Figure 6 shows the composite graph of the plasma protein determinations in each group of patients. Here a striking difference is observed in the response of the two groups. Each curve fell sharply immediately after admission of the patients to the hospital as adequate hydration was obtained by the employment of parenteral fluids. In the course of treatment, however, the plasma protein curve of those patients who survived rose rapidly to normal and even unusually high levels, whereas, the composite curve of those patients who succumbed failed to show this response. These later observations correspond to those in the experimental study in which it was observed that the plasma protein curve of the Group I dogs

which survived maintained a better than average height, whereas, the curve of the Group II dogs which succumbed fell consistently.

Corroboration of the impressions conveyed by the composite graphs may be had by an examination of Figures 7, 8, 9, and 10, which show the hematocrit and plasma protein curves of each of 4 patients. Graphs of patients who survived are shown in Figures 7 and 8. Comparatively large amounts of citrated blood were given to each child, and the plasma protein response was striking. Graphs of patients who succumbed are found in Figures 9 and 10. In each instance the hematocrit curves were maintained at a high level by the frequent transfusions, but there was no like response on the part of the plasma protein which remained at subnormal levels until the death of each patient. The patient whose graphs are shown in Figure 9 was an adult male, who, undoubtedly, received transfusions of blood too infrequently and in too small quantity. It is a matter of speculation whether or not larger and more frequent transfusions might have raised the plasma protein level to normal, thus influencing favorably the ultimate outcome. The patient represented by Figure 10 died in spite of comparatively large

and frequent transfusions and her plasma protein level though rising had never reached a normal point. It is interesting to note that 2 of the patients became quite edematous before death. In each instance this followed the judicious use of sodium chloride administered intravenously.

CONCLUSIONS

Although the number of experimental animals and of patients observed during this study is comparatively small the data accumulated have been so consistent in certain respects that they were deemed worthy of report, particularly since there seems to be a justifiable practical application.

In experimental *Staphylococcus septicemia* in dogs there was a marked fall in the hematocrit level both in animals fatally ill and in those ultimately recovering. Patients afflicted with *Staphylococcus septicemia*, whether they survived or died were able to maintain normal hematocrit ranges with the aid of numerous transfusions.

In untreated experimental animals and in patients undergoing intensive therapy a distinct line is drawn by plasma protein levels between those (animals and patients) who survived and those who succumbed. The plasma protein curves of the former maintained or reached a better than average level whereas the curves of those who succumbed steadily fell or failed to rise even in the instance of the patients who received intensive treatment including numerous blood transfusions.

It is our belief that these observations are a sufficient basis for considering the plasma protein levels observed clinically in *Staphylococcus septicemia* as a valuable prognostic aid. It would appear that the plasma protein level

falls in all patients having *Staphylococcus septicemia*, but that in those instances in which recovery is to occur the proteins rise and are maintained at a high point after adequate therapy. Since it has been shown that the plasma protein responds more slowly to repeated transfusions than does the hematocrit, the former should be used as a therapeutic guide to indicate the need for blood transfusions. Large amounts of whole blood or plasma, repeatedly administered, give the greatest opportunity for recovery.

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CHEMOTHERAPY AND ROENTGEN RADIATION IN CLOSTRIDIUM WELCHII INFECTIONS

Clinical and Experimental Studies

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CLINICAL clostridium infections range in severity from relatively benign infections to more fulminating and malignant types. The etiological organism may be either *Clostridium welchii*, *Clostridium septicum*, or *Clostridium oedematiens*, or a combination of the three. Our present clinical and experimental studies are confined to *Clostridium welchii*, for this is by far the most common offender clinically.

There is doubt in the minds of many as to just what "gas gangrene" really is. The present controversy over the proper therapeutic measures leaves no doubt that many criteria may be loosely interpreted. The term "gas cellulitis" or "clostridium cellulitis" is suggested not to supplant the term "gas gangrene," but to provide a hitherto missing category in which to place the milder, the borderline, and the atypical case.

We have come to give less credence to the term "gas gangrene." Does such an entity really exist, or does it simply include the more fulminant cases of clostridium cellulitis? "Cellulitis," either used or implied, is a more inclusive term and is perhaps more apt in emphasizing the bacterial origin and nature of the infection. There are cases that have become fulminating within several hours, and there are other cases which have developed slowly. The infection may extend largely in both the subcutaneous tissue and muscle in another, even though both patients are equal-

ly sick. There have been a few cases of superficial *Clostridium welchii* infection with persistently positive cultures, at times with small amounts of gas in the immediate vicinity but with an essentially benign course. These latter cases have been excluded from the present series even though we believe that they are milder manifestations of the same infection.

It is possible that the disease which we are accustomed to see differs in some way from the classical description. Definite muscle involvement is usually not proved now that more conservative measures are used. In our study, therefore, the criteria for calling cases "gas gangrene" are (1) positive cultures of *Clostridium welchii*, (2) spreading infection, (3) gas in the tissues, and (4) discoloration and edema of the involved structures (17). One of our first concerns has been to establish the presence of a true "gas gangrene." Regardless of whether or not this is done, any spreading infection with *Clostridium welchii* found in the culture, or any infection with gas in the tissues has been treated as a severe case. If the four criteria were not all met, the case was not included in our series. Among those omitted were 4 simple *Clostridium welchii* infections, 2 of which presented small amounts of gas in the tissues (Table I). In 2 additional cases, crepitus was noted but no *Clostridium welchii* were found. The offenders were *Escherichia coli* in one case, and in the other an anaerobic streptococcus and a hemolytic staphylococcus.

CLINICAL EVALUATION OF PRESENT THERAPEUTIC AGENTS

Sulfanilamide, sulfapyridine, sulfathiazole,
roentgen irradiation, antisera, zinc peroxide

TABLE I—CLINICAL WOUND INFECTION WITH CLOSTRIDIUM WELCHII

Name	Age	Case	Treatment	Result
W. B.	27 yrs.	Mangled forearm	Sulfonamide, irradiation	Well
J. W.	25 yrs.	Mangled forearm	Irradiation	Well
W.	3	Infected heel	Irradiation	Well
R.	24 yrs.	Cythrosis of lower back abscess	Sulfonamide, irradiation	Dead (wound closed)

pastes, and the inhalation of high concentrations of oxygen have each been recommended recently for the treatment of *Clostridium welchii* infections. The multiplicity of these agents and the disparagement which each in turn has received implies that a method of appreciable superiority is still wanting. On the other hand, the mere fact that no one is advocating a continuation of the previously prevalent radical surgery suggests that the various sulfonamide drugs, roentgen irradiation or the antiserum may each favorably modify the course of the disease. We believe that the diversity of opinion regarding the relative merits of any one of these therapeutic agents may in part be due to the wide variation in the severity of this type of clinical infection that is a true "gas gangrene" as here defined or a *clostridium cellulitis*.

Antiserum. The polyvalent antiserum, in efficient at best when used alone, can easily be proved to be of some value experimentally (10-13). In mice and guinea pigs it is more efficacious than is sulfanilamide. In clinical use the polyvalent antiserum gives acceptable results when used with conservative surgery, but prophylactically its effect is feeble (1-14). That this should be so follows rationally when one compares the antiserum for *clostridium* infections with the antiserum for tetanus. In the latter disease the antiserum combats, and very effectively, the tetanus exotoxin which has a systemic effect while the action against the usually insignificant local lesion is minimal. The local source of infection is usually small and tends to heal itself.

In the case of *Clostridium welchii* infections, the antiserum may well control the exotoxins distributed throughout the body but these are of far less magnitude than is the virulent local lesion which progresses rapidly killing

more tissue and forming exotoxins far in excess of the amount that the polyvalent antiserum can control.

In prophylactic use the same situation holds. The tetanus antiserum neutralizes the exotoxins as they are liberated from the small local wound. In *Clostridium welchii* infections, the local lesion tends to spread often rapidly regardless of the systemic effect of the exotoxin. Therefore, the *welchii* antiserum could act through its effect on the local lesion immediately adjacent to the wound. At best it could only slow down the advancing necrosis.

For these reasons we do not insist on the use of *Clostridium welchii* antiserum either prophylactically or therapeutically. We have used it but twice in our last 18 cases. It is important to note however that the protective action of the antiserum in small animal experiments is far greater than it is in humans.

Surgery. In contrast to the past, the need for amputation now is dictated not as much by the infection as it is by the state of the vascular bed. The coexistence of vascular damage to an extremity plus a *Clostridium welchii* infection has often distorted the picture. The infection was held mainly to be responsible for not only the gas, edema, and seropurulent exudate, but also for the massive necrosis, discoloration and particularly malignant course. While the radical measure of amputation is still accepted in this extreme there is no question but that a wound infection with only *Clostridium welchii* or with other contaminants too may run an exceedingly indolent course. When in the muscle (deeper wounds) the progression is more rapid and more serious and there is evidently a distinct local necrotizing effect of the toxin. However this is shared by other organisms and is seen not infrequently. Perhaps the most common of the others is the cellulitis caused by the streptococcus. The opportunity for growth of *Clostridium welchii* not shared by the other organisms is the remarkable ability to form gas. This may facilitate the dissection along fascial planes and cause a certain amount of pressure to be exerted.

The contrast between the classical picture of a gas gangrene and many of the wounds

TABLE II—TRUE CLINICAL GAS GANGRENE
(MORTALITY 33.3 PER CENT)

Name	Age	Cause	Treatment	Result
A S	44	Compound fracture amputation	Irradiation, anti serum sulfanilamide	Slow recovery
T W	85	Arteriosclerotic gangrene amputation	Irradiation sulfa nilamide	Dead
W D	70	Diabetic gangrene amputation	Irradiation sulfa nilamide	Dead
C M	46	Compound fracture débridement	Irradiation	Living
W J	68	Arteriosclerotic gangrene	Minimal sulfanilamide irradiation	Dead
F K	62	Arteriosclerotic gangrene amputation	Irradiation	Slow recovery
C N	9	Surgical scarlet fever of arm	Irradiation sulfa nilamide	Well
J M	46	Abscess of leg	Sulfadiazine	Well
J W	18	Compound fracture of forearm	Irradiation sulfa diazine	Well

TABLE III—CLOSTRIDIUM WELCHII INFECTION
OF ABDOMINAL WALL WITH TISSUE NECROSIS OF GREAT EXTENT

Name	Age	Cause	Treatment	Result
J M	50	Perirectal abscess diabetes	Irradiation, anti serum sulfanilamide drainage	Living
J M	72	Extravasation of urine syphilis	Irradiation sulfa thiazole drainage	Living
A M	62	Ruptured appendix	Irradiation sulfa nilamide drainage	Living
S M	72	Strangulated hernia	Irradiation sulfa nilamide drainage	Living
C T	32	Intestinal obstruction enterostomy	Irradiation sulfa nilamide	Died 3 days
J H	17	Carcinoma of testicle	Irradiation sulfa nilamide	Died 30 days after treatment

seen in civil life suggests that there are many of these infections which might be called "clostridium cellulitis" or "gas cellulitis". Many of the latter are quite fulminant, and easily fulfill the criteria of a "gas gangrene". However, the presence of a relatively intact vascular bed leads to conservative measures

In arteriosclerotic gangrene and in similar infections, amputation is going to be necessary in a number of cases regardless of whether a Clostridium welchii infection is present or not. Therefore, it is too much to presume that any measure will cure the infection at a site where the part is unable to survive even without the infection. The appearance of the disease in a stump following amputation may well be treated conservatively by simple drainage measures plus one of the sulfonamides or roentgen irradiation, rather than by higher amputation. This is assuming that a relatively intact vascular bed is present in the stump.

In the traumatic cases in which there is considerable destruction and mangling of the tissues (and again assuming that there is no great arterial damage), the infections may safely be treated conservatively. With adequate drainage (we do not use débridement although many advocate it) and the use of roentgen irradiation or a sulfonamide, we believe that we have obtained good results.

Roentgen irradiation. In this series we have included every patient who has been in the

Strong Memorial Hospital with "gas gangrene" since 1937 (Tables II and III).

Roentgen irradiation has a definite beneficial effect on the course of the disease. During the last 4 years we have seen fit to use this agent in all but 1 of our cases. In several instances the response to irradiation has been clearcut since no other therapeutic measures were being taken at the time (17).

On the other hand, our results with roentgen irradiation have not been as good as have those of Kelly (11). There have been 5 deaths in our series of 15 cases of "gas gangrene". One of these (C T, Table III) was a frank therapeutic failure. Another death occurred 30 days after the infection had been controlled and treatment had been stopped. Since death was caused by an advanced carcinoma of the testicle, perhaps this case should not be included as a failure.

The remaining 3 deaths occurred with considerable similarity in patients 68, 70, and 85 years old in whom the general physical condition was poor (Table II). The Clostridium welchii infection did not seem to have any more bearing on their demise than did co-existent pneumonia and advanced arteriosclerosis. Two of these 3 patients had recently suffered amputations because of arteriosclerotic vascular disease of the legs. On the other hand, there have been several reports of distinctly unfavorable outcomes (6, 7). Caldwell's studies of the effect of irradiation on guinea pigs led him to believe that irradiation



Fig. 1. Photograph of control dog 30 days after inoculation.



Fig. 2. Photograph of dog treated with sulfadiazine 10 days after inoculation.

was of extremely little value (5). More recently a series of studies of compound fractures contaminated by *Clostridium welchii* were reported (4). In that series, all of his control animals died while 30 per cent of the treated animals survived.

Sulfonamides plus roentgen irradiation. Is the use of both irradiation and a sulfonamide advisable? Until recently there has been no clinical or experimental proof that these two should not be used together. It has been suggested that the combined use is contra-indicated (11, 12). Until the last few months we had assumed perhaps unjustifiably that the measures were probably complementary. The majority of our patients were given either roentgen irradiation plus sulfanilamide or roentgen irradiation plus sulfadiazine with success. As we see only 3 or 4 clinical cases of *Clostridium welchii* infection a year it is impossible to present a series of any significant size. However if we assume that our method of approach in dogs is reasonably comparable roentgen irradiation plus sulfadiazine gives poorer results than does either one alone (Table IV).

Sulfonamides. Although the use of the sulfonamide drugs is in favor only a few small series have appeared (2, 17). These have been treated mainly with sulfanilamide. Our experience is not conclusive since most of our patients have been treated predominantly by irradiation, and more recently by sulfadiazine.

Sulfanilamide was used in 10 earlier cases because we believed that it might prove to be an adjunct to roentgen irradiation. In the few instances in which the patient was maintained on the drug alone for a reasonable period before irradiation was started the infection was not brought under control.

These scattered clinical impressions are borne out fairly accurately by the experimental results. Four observers (3, 4, 9, 10) have found that in guinea pigs there is a distinct protective action and some curative effect by the drug. Others disagree but admit that sulfathiazole has some effect (15). Sulfathiazole is more efficacious than either sulfanilamide or sulfapyridine (10, 15) and again the best experimental results were obtained by local use. No reported series is yet available but Wilson mentions that sulfathiazole plus antiserum and conservative surgery are being used predominantly on these infections in England at present. One patient that we treated with both sulfathiazole and roentgen irradiation made a satisfactory recovery.

We have given sulfadiazine to 3 patients with *Clostridium welchii* infections in addition to applying it to the local lesion. In each case the infection was brought under control rapidly and within 2 to 3 days clean granulations covered a good portion of the affected area. One of these patients received nothing at any time but sulfadiazine while in the other 2 this was supplemented by roentgen

irradiation One of the latter died from other causes

EXPERIMENTAL CLOSTRIDIUM WELCHII INFECTION IN DOGS

Roentgen irradiation in clostridium welchii infections was used for about 6 years before there was any experimental confirmation of its action. In large part this was due not to a lack of effort, but to a lack of adequate proof. Our first year of laboratory investigation was conducted on guinea pigs. We were not able to produce a satisfactory facsimile of a human "gas gangrene" because the spread through the tissues was so rapid that it became a generalized disease rather than a local one so that local roentgen irradiation was not effective. The irradiated group did a little better than the controls but the results were not statistically significant.

For an experimental test of the effects of roentgen irradiation and chemotherapy, we have produced Clostridium welchii infection experimentally in 255 dogs. This results in an infection which is quite similar to the disease in humans and is one which progresses somewhat more slowly through the tissues than it does in smaller animals (8). The disease was produced by injecting 1 to 2 to 15 cubic centimeters of a 20 hour, deep meat, subculture of a single strain deep into the thigh muscles. This strain was from a fatal case of Clostridium welchii infection and had remained undisturbed in an icebox for 6 months. By taking the subculture each week from this master culture we were able to minimize the changes in toxicity and virulence that one working with these preparations must contend with.

Usually within 3 hours after injection, there was edema and tenderness of the thigh with gas palpable deep in the tissues. When undisturbed, the infection progressed rapidly. It dissected into the lower thigh and up into the abdominal wall usually with a fatal result in 24 hours.

Roentgen irradiation Of the 89 animals in the irradiation group, 50 received roentgen irradiation after the infection had become established (therapeutic irradiation), and 39 were kept for controls. The experiment was

TABLE IV — COMPARISON OF SULFADIAZINE, IRRADIATION, AND COMBINATION OF TWO USED THERAPEUTICALLY IN DOGS WITH CLOSTRIDIUM WELCHII INFECTION

	No	Survivals	Per cent
Roentgen irradiation			
Controls	50	13	26
Sulfadiazine	39	7	17.9
Controls	25	7	28
Sulfadiazine plus roentgen irradiation	15	1	6.7
Controls	25	3	12
	12	3	25

carried out in groups of 4 to 10 dogs injected simultaneously. Of the irradiated animals, 26 per cent survived (Table IV), and of the control group, 17.9 per cent survived. From the experimental standpoint, roentgen irradiation would not seem to be logical as a prophylactic measure.¹

Sulfadiazine and roentgen irradiation When sulfadiazine combined with roentgen irradiation was given after the infection was well established in 25 dogs, there was a survival of only 12 per cent (Table IV). We have no explanation for this apparently antagonistic effect between roentgen irradiation and sulfadiazine. Work in progress may clear up this paradox. For the present we offer it only as preliminary evidence that the two methods are not complementary and should not be used in conjunction with each other.

Sulfonamides Our experience with sulfanilamide in dogs is comparable to that of other workers in this field. When used *prophylactically* (if the concentration of the drug in the blood is raised to therapeutic levels prior to the inoculation with the infectious agent), sulfanilamide gave a survival of 60 per cent in 15 dogs. Under the same conditions, butryl sulfanilamide (a highly soluble preparation of sulfanilamide) gave 30 per cent survival out of a group of 10 dogs, while of 37 dogs in the control group, there was only a 16 per cent survival (Table V). When sulfanilamide is used *after* the infection is established, the advantage over the control group should be considerably less as judged by our results with

¹The same group of controls has frequently been used for one or more experiments run concurrently.

TABLE V.—CLOSTRIDIUM WELCHII INFECTION IN DOGS TREATED PROPHYLACTICALLY

	No.	Survivals	Per cent
Controls	37	6	16
Betacyl sulfanilamide	30	3	30
Sulfadiazine	5		60
Sulfanilamide	25	15	60

TABLE VI.—SULFADIAZINE TREATMENT OF DOGS AFTER CLOSTRIDIUM WELCHII IS ESTABLISHED

	Dogs	Survivals	Per cent
Sulfadiazine	15		67
Control	5		2

sulfadiazine. Other variations of the technique suggest that the drug used locally is a little more efficacious than when given parenterally. In view of the results obtained with sulfadiazine the prophylactic value of these two drugs was not sufficient to warrant a therapeutic test on dogs.

These results are fairly consistent with the reports of others for *Clostridium welchii* infection but with *Clostridium septicum* and *Clostridium oedematis* there is considerable contradiction (9, 10, 16).

Sulfadiazine. Sulfadiazine has been superior in our hands to other drugs. When used prophylactically in 25 dogs with experimental *Clostridium welchii* infection, there was an 83 per cent survival. The control group of 37 dogs (the same used in the preceding group) presented a 16 per cent survival. As shown in Table V this is appreciably better than any results we had obtained with sulfanilamide preparations. After the infection was established in 25 dogs, the sulfadiazine was given therapeutically (3 hours after inoculation) and there was still a 67 per cent survival. This is in contrast to a survival of 6.7 per cent of 15 control dogs run concurrently (Table VI). None of the procedures used has actually aborted the infection.

In the prophylactic experiments with sulfadiazine many of the animals showed none of the toxic symptoms which we were accustomed to see. The dogs would often feel well enough to walk about instead of lying prone

in their cages. The accompanying photographs (Figs. 1 and 2) show the difference between a control and one of the sulfadiazine treated dogs at the end of 10 days.

CONCLUSIONS

From our experience it seems that a number of cases of *Clostridium welchii* infection fall awkwardly into the group called "gas gangrene." For this group the term "clostridium infection" seems rather inadequate but "clostridium cellulitis" is a reasonably descriptive term. There is undoubtedly a wide variation in the manifestations of the disease.

The complementary use of conservative surgery with either a sulfonamide or roentgen irradiation gives as good results as we know how to obtain at present. The reservation of amputation for these cases in which there is a markedly compromised vascular bed is warranted.

Both sulfanilamide and roentgen irradiation when employed alone have some beneficial effect on the course of the infection both experimentally and clinically, and lately we have used sulfadiazine in 3 patients with success. All of these observations are borne out more or less clearly by animal experimentation. The results have been especially encouraging with sulfadiazine. The prophylactic use of the sulfonamides is invariably superior to administration of the drug after the infection is under way.

The development of the experimental aspects of the studies has been delayed by the variance of strains, loss of virulence and by the multiplicity of therapeutic measures used. All of these variables must be considered in grading experimental results.

We believe that it is essential particularly in the study of this infection to reproduce a disease which resembles closely that seen in humans. In our hands this ideal has been more nearly fulfilled in dogs than with any of the other laboratory animals. The resemblance is closer to the human reaction in all respects. As seen from the charts, there are always a few of the controls that survive (6.7 to 25 per cent) but there has always been a

100 of nonoperative control dogs, the average survival has been 24 per cent.

Anyone familiar with the use of sulfathiazole is aware of the various manifestations of drug intoxication. These include fever, rash, and conjunctivitis chiefly, nausea and blood destruction do not occur so frequently. All of these phenomena were observed in the present series, and on a few occasions it was necessary to discontinue the drug, but this happened in only 1 of the 5 fatal cases.

Table II offers an interesting comparison. Despite the smaller size of the second group certain remarks may be made. I believe that the low incidence of deaths from generalized peritonitis is due to the effect of sulfathiazole, and in the cases of the 2 patients who succumbed the postoperative course was prolonged far beyond the most optimistic expectations.

The absence of deaths resulting from unrecognized mechanical ileus or from unrecognized subphrenic abscess is not due to the lack of these complications, for they occurred with their usual frequency, nor can the fact be ascribed solely to the use of sulfathiazole. It is in this group of patients, with complications treated inadequately in the earlier series, that better methods of postoperative care have brought about improved results.

The single patient considered to be inadequately treated was a 7 year old boy who had generalized peritonitis of appendical origin. He improved steadily for 8 days after opera-

tion, and then a definite pelvic abscess formed. This was recognized, but palliative therapy was attempted rather than surgical drainage. On the thirteenth day after operation the abscess suddenly ruptured, and the patient died in a few hours.

That no deaths occurred from pneumonia is probably the result of the chemotherapy.

The single fatality placed in the "poor risk" category was that of a male of 58 years who entered the hospital with generalized peritonitis and in acidotic coma. He was found to have diabetes mellitus, and the blood contained 460 milligrams per cent of sugar. Efforts to regulate the diabetes and to improve his condition generally were unavailing. He died 2 days after operation.

In summary, it can be fairly stated that sulfathiazole given by vein or by mouth is a useful adjunct to the treatment of perforative appendicitis. An equally potent factor in the improved results obtained in the Johns Hopkins Hospital during the past 2 years has been the more adequate treatment of postoperative complications. Although this series of cases is small, the trend is in the right direction and serves to strengthen my conviction that immediate operation is the correct treatment for acute appendicitis in any stage of the disease.

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THE VALUE OF SULFATHIAZOLE IN THE TREATMENT OF PERITONITIS AND ABSCESES OF APPENDICAL ORIGIN

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IN a previously reported series (1) of 479 consecutive cases of peritonitis or abscess of appendical origin in all of which the condition was treated at the Johns Hopkins Hospital by immediate operation, there were 48 deaths, a mortality rate of 10 per cent. This mortality rate compares favorably with those reported from other hospitals of similar size and is somewhat lower than the average of results reported for the delayed or expectant treatment of perforative appendicitis. A study of the fatal cases, however, showed that at least 14 of the deaths were the result of inadequate diagnosis and treatment of complications which arose days or weeks after the initial operation.

Since then 2 years have elapsed, during which period a second group of consecutive cases has been treated. This series although numerically smaller resembles the earlier one exactly as regards type of patients, proportion of appendical perforations on admission and incidence of the various postoperative complications, but less than half of the expected number of deaths occurred. The treatment of the patients in this second group differed from that of the earlier series by the use of sulfathiazole in nearly all instances, and by more careful observation and treatment of those patients who did not recover promptly after operation. As in the earlier series, every patient was subjected to immediate operation. From September 1, 1939, to September 1, 1941 there were 105 patients who had peritonitis or abscess of appendical origin and only 5 of them died. Postmortem examination was made in 4 of these.

Others have reported on the use of sulfanilamide and related drugs in the treatment of perforative appendicitis, and in most instances the drugs have been used locally in the wound,

or in the peritoneal cavity. In the present series of cases sulfathiazole was administered intravenously and/or by mouth, none being used locally. It was desirable to give this method a thorough trial so that an evaluation could be made and it seemed that spreading infections and infections of extra appendical origin, such as pneumonia, might be more effectively dealt with in this manner. An initial dose of 4 grams of sulfathiazole was given to the average adult, and this was followed at regular intervals by a sufficient amount of the drug to maintain a level in the blood of 6 to 8 milligrams per cent. The first dose or two was usually administered intravenously and thereafter the drug was given by mouth unless it was found that the patient was unable to retain it.

TABLE I.—GENERAL SUMMARY OF RESULTS

	No. patients	No. deaths	Per cent
Appendicitis with perforation and abscess	42	—	.23
Appendicitis with perforation and peritonitis	63	4	6.35
Totals	5	4	4.76

TABLE II.—CHIEF CAUSES OF DEATH

	No. deaths from (1) 1939-1940 consecutive patients	No. deaths from (2) 1941-1942 consecutive patients
Causes of death		
Direct complication of appendicitis		
Generalized peritonitis	3	—
Pyelonephritis	4	—
Septicemia	—	—
Mechanical ileus	7	—
Subphrenic abscess	5	—
Retrovesical fistula	—	—
Spontaneous rupture of untreated pelvic abscess	—	—
Extra-appendical complications		
Cerebral accident	—	—
Pulmonary embolism	3	—
Pneumonia	4	—
"Poor-risk" patients	4	—
Cause of death uncertain	4	—
Total	43	5

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The contribution made by Winnett Orr when he pointed out the importance of wide open drainage, complete immobilization, and infrequent dressings cannot be overestimated. These wounds do not need to be dressed for 2 or 3 weeks and by that time are completely lined with healthy granulations and are well on the way to closure.

When the importance of this principle was thoroughly understood, a great change came into the treatment of the septic nonunions. Instead of limiting treatment to the infection and the osteomyelitis and waiting a year or two before attempting a bone graft operation, it became the general practice to deal with the nonunion at once by removing the sequestra, placing the freshened fragments in contact and immobilizing. The result in almost all cases was a quick union of the fracture and the saving of a year or two of hospitalization.

NERVE LESIONS

Of all the problems that the war brought to the reconstruction hospitals the most interesting was that of the lesions of the nerves. These cases were collected in special hospitals because in them the surgical staff was composed of men specially trained in extremity surgery and particularly qualified to deal with the deformities and disabilities that result from nerve lesions.

The rise of the neurological surgeon may lead to some agitation for a transfer of the nerve lesions from the orthopedic to the neurological surgeon, but from my observation of the two types of surgeon in action and from my own experience with both types of surgery, I would say that these patients are more likely to profit in the long run from the care of the modern orthopedic surgeon than from any other.

The lessons we learned about the wounds of the nerves were of the utmost importance and should be reviewed now if our young surgeons are to avoid our mistakes. Let me say that of all the remarkable things the surgeon does none is so spectacular in its results as the suture of a nerve. On the other hand no operation requires more attention to the details of technique if the best results are to be obtained.

Both in military and in civilian practice the question often arises as to whether a suture of a severed nerve should or should not be performed at the preliminary débridement. My answer is that if speed is necessary because of shock or hemorrhage or if there is the slightest risk of infection it should not be done. In clean incised wounds in which a thorough clean-up can be carried out it is justifiable, but in a shell wound, never. The business of the surgeon is to do a débridement as quickly and thoroughly as possible and to get the patient into an efficient splint and back to bed or on his way down the lines. The most that should ever be done to a severed nerve is to link the two ends with a catgut suture so that when the ultimate dissection is done the ends will be found close together.

The technique of nerve suture is well known, but I cannot refrain from referring to the absolute necessity of getting end-to-end contact if recovery is to be expected. To accomplish this all sorts of tricks must be resorted to, such as transferring the ulnar in front of the internal epicondyle and flexing the elbow acutely, flexing the knee to a right angle while repairing a 6 inch gap in the sciatic nerve and then placing the patient on his back with his hip in full extension and his leg dropped through a hole in the mattress so as to relieve tension on the sutures. In all these operations in which joints must be held flexed after the suture, a plaster bandage must be applied and left undisturbed for at least a month, that is, until the down-growing axis cylinders are well past the line of suture. After that a series of plasters must be applied at weekly intervals, and the joint straightened out gradually.

Occasionally the surgeon is confronted with a lesion in which the gap is so great that there is no hope whatever of bringing the severed ends into contact. If this happens in the musculospiral nerve it is of no great consequence because one can count on an extraordinarily good result from a transfer of flexor muscles into the extensors. But when it occurs in the median nerve it is a major calamity. Here there are three alternatives. First, one may dissect the nerve a long way back and then draw the two bulbs as closely together as they

SOME LESSONS LEARNED IN THE GREAT WAR

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TO those of us whose fortune it has been to serve our troops in time of war the spectacle of what is happening in Europe today cannot fail to make vivid again the memories of what we learned and to stir within us anew a burning desire to help our heroic men. If we are to be truly helpful however we must make sure that we have really remembered the lessons we learned and that we are prepared to apply to present war conditions all the lessons that are new.

In approaching this important subject one is apt to succumb to the temptation to comment on every field of surgery with which one has had any contact whatever. Thus it is with difficulty that I refrain from referring to the remarkable things that we saw and did in the gunshot wounds of the chest, abdomen and skull. On this occasion however I shall confine myself strictly to that field in which I have had a really broad experience and in which I should be able to speak with some authority.

Thinking over the compound fractures of the bones of the extremities, I would say that the greatest advance came from the introduction on the battle field or at the ambulance dressing station of adequate splinting. Every body knows the spectacular reduction of the mortality rate that came with the introduction of the Thomas splint. Similarly there came a great improvement in the final results when the new methods of applying traction, such as by ice tonges, Sinclair's skates, and other devices were introduced. I have no doubt that further improvement will result from the Kirschner wire.

The outstanding impression left on my mind however from observation of large numbers of these patients at the convalescent stage was the very great difference in the quality of the results obtained in different hospitals. The explanation was perfectly sim-

ple for in one there was a leading spirit like Sinclair or Pearson or Blake whereas in another there was nobody interested in fractures. Surgeons had better get over the idea that anybody can treat fractures well enough, for the results that come from incompetent management are appalling. The remedy of course, is to see that at least one expert in fractures is attached to each surgical unit.

The most important contribution to the treatment of wounds in the last war was the preliminary débridement followed by the Carrel Dakin method of irrigation. Whether the latter will be superseded by the new methods remains to be seen. With regard to these, however it would seem that if the bombing would allow a controlled experimental study of the new methods such as the Trueta or closure treatment and the local and general use of the sulfonamide drugs, some definite conclusion should be arrived at before long. As things stand at present there is very little reason for confidence in the statements that are being made either for or against their use.

While practically all the compound fractures resulting from gunshot became infected, osteomyelitis was not a serious complication nor did it interfere greatly with the final result. Union went on in the usual way and of ten with greater osteogenic activity in the fragments than in simple fractures. Before my war experience it had always been my impression that infection was an important cause of nonunion. As an actual fact, however of a thousand infected compound fractures that passed through my hands, less than 50 failed to unite and when one came to investigate these one found that the nonunion in most cases was due to loss of bone.

The most important lesson learned in regard to chronic osteomyelitis and septic nonunion was that the patients could be operated upon without any serious risk of stirring up the infection and that if the wound was left wide open with gauze drainage extending into its depths they rarely had a rise of temperature.

is well fitted on the ends of the sectioned bones, and if the nerves are cut well back, it will stand up to hard usage for a lifetime

One of the chief causes of the unpopularity of the Syme operation has been the unfriendliness towards it of the artificial limb makers. Not many of them can make a good Syme artificial limb and even when they can they dislike it because it cannot be made symmetrical with the opposite limb. The result has been that whenever a Syme stump is the least bit defective, off it comes to make way for the pretty below-knee artificial limb. Unfortunately many a man has lived to rue the loss of his Syme stump for it is rare indeed for the midcalf below-knee stump to stand up to the wear and tear of ordinary usage the way a Syme's will do. The trouble with the below-knee stump is that with each step the whole of the weight is borne on the sloping sides of the upper end of the tibia, on skin that is unaccustomed to intermittent pressure and friction. The result is a succession of attacks of skin irritation, blistering, and ulceration. In not 1 in 10 cases can these men face anything but a sedentary life.

When the unsuitability of the midcalf operation for Canadian soldiers became apparent, all enthusiasm for reamputating Syme's stumps disappeared. It was quickly discovered that many of the defects could be overcome by doing the Syme operation over again, refashioning the flap, cutting short the nerves, and making sure that the bulbous soft tissue pad was held in correct relationship to the bones until healing occurred. Over and over again these defective stumps have been made perfect in this way and there is no doubt that before any Syme stump is amputated the possibility of repairing it should be thoroughly considered.

So unsatisfactory has the below-knee amputation proved in the Canadian army that the majority of these stumps, after a series of reamputations, removals of the fibula and excisions of neuromas have finally been converted into Gritti-Stokes above-knee end-bearing stumps. It is a pity, of course, to have to sacrifice the knee joint but experience has shown that the end-bearing thigh stump is far more serviceable to the workman than the

midcalf. Large numbers of our men with this type of amputation are working an 8 hour day at benches and machines and seldom losing a day's work.

Compared with the other amputations that of the midthigh is a great calamity. In spite of the amazingly clever artificial limb that has been devised for it, it has been found that the men are rarely able to hold any but sedentary jobs. The trouble is that they have to sit on the top of the bucket, carrying weight on skin that is not accustomed to it and with only the minimum of control over the movement of the joints. It should be performed, therefore, only as a life-saving measure.

The dictum of Ambroise Paré that a gunshot compound fracture, combined with a rupture of the main artery to the limb, calls for amputation has stood for nearly 400 years. We are wondering, however, if after all this time some exceptions may not be found to this rule. Paré was faced with the certainty of infection piled on top of the fracture and the severe injury to the circulation so that he knew that his patient's only chance depended on an immediate amputation. With early débridement of wounds, however, infection can be completely prevented in many cases and the new drugs may ultimately increase this number. It may be possible, therefore, with the aid of heparin, to restore the circulation at the time of the débridement by suture of the severed artery or to maintain it for a few days by means of a glass tube, until a collateral circulation is established. Certainly the experimental studies of Murray both on animals and on a small series of patients in hospital indicate that occasionally, particularly in air raids, when the patients can be brought quickly to hospital, such a plan of treatment might be effective.

While in this review of experiences gained in the war of 1914 I have limited myself to a very small part of the broad field of war surgery, much of what I have said has close relationship to all wounds, no matter where they may occur. What we all want to know is, first, how to prevent wounds becoming infected and, second, if they are already infected when they come into our hands, how best to combat that infection and to give our patient

will come with a silk thread, and close the wound. Ten days later the wound can be opened up and it will often be found that the ends can then be brought together without tension. Second one may introduce a nerve graft. Theoretically this should be useful for it has been done successfully in animals, but in man the results have been disappointing. In no case in which I saw it done was the result worth the trouble. However if I were working on these cases now I would try out the suggestion of using degenerated nerve as a graft and freshening the distal end and the proximal end of the distal segment of the nerve when the axis cylinders were due to pass that point. This would at least be more hopeful than the third alternative which consists of doing nothing.

AMPUTATIONS

Familiar as most surgeons are with the various types of amputations not many have had a sufficient experience to justify the formation of final opinions on all phases of the question. It happens, however that it has been the policy of the Canadian Government to bring all the amputation cases from time to time to an amputation clinic at the Government artificial limb factory at Toronto so that it has been possible for a small group of surgeons, of whom I am one to study and to follow these cases for nearly 25 years. A life history of all these patients, comprising 2,000 in all, is now being prepared by Dr. Gordon Dale and will be published soon. From our place of vantage in this clinic we have been able to observe these men not for a week or a year but for a quarter of a century. We have figuratively watched them walk down the years, slowly changing from youth to old age and we feel that we know as few can possibly have had the opportunity to know the surger of amputation.

I shall not attempt to discuss this matter in any detail as this has recently been done elsewhere. I must point out however a few outstanding principles that it would be well to remember if it is our misfortune to have to face again the casualty lists of 1918. Almost the only reason for amputating a soldier's limb is to save his life. It is because his limb is

gangrenous or about to become gangrenous because of wildly spreading streptococcus or gas bacillus infection. It is seldom, therefore that a formal amputation of any kind is justifiable. One must content oneself with a quick circular cut, leaving the skin long so that it cannot retract above the section of the muscles and bone and leaving the wound wide open for adequate drainage. This is the so-called guillotine amputation, modified by leaving the skin long that became so popular in the casualty clearing stations and base hospitals in the old war. It was a life saver pure and simple, but it worked.

One sometimes hears this type of amputation criticized on the grounds that it takes the stump a long time to heal that it usually leaves a stump that is unsuited to fitting with an artificial limb and that it often requires re-amputation. Admitting the truth of all these criticisms, however we are still convinced that this method must be used if the mortality rate is to be kept down. Some modification of these views may come if the new bacteriostatic drugs prove helpful, but I doubt it.

It is in the reconstruction hospitals that final preparation of these patients for artificial limbs takes place and it is here that the formal amputations should be done. In the lower extremity there are only four that need concern us as the others are practically only of historical interest. They are the Syme's and the midcalf operations below the knee and the Griggs-Stokes and the midthigh above.

For nearly a hundred years the academic storms have raged about the operation of Syme. At one time it used to be the London surgeons who abused it but now it is said that Edinburgh has forsaken it and London has taken it up. Our experience has been, however that it is the best of all amputations of the lower extremity and that when well done it allows a man to stand and walk all day to follow the plough, to work in a factory or to do most of the things that a normal man can do. Twenty years ago I was put out of a squash tournament by a man who had had a Syme amputation done 15 years before. I met him the other day 35 years after his operation walking along with hardly a sign of a limp. It is our experience that if the heel flap

is well fitted on the ends of the sectioned bones, and if the nerves are cut well back, it will stand up to hard usage for a lifetime

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the best chance for his life and limb. From the old war we learned or relearned the importance of splinting, débridement, and free drainage. In this war we shall have an opportunity to try out the effectiveness of chemotherapy and the use locally of the sulfonamide group of drugs. If medical experience in this war in any way resembles that of the last, however, the process of arriving at sound conclusions on these matters will be exceedingly slow. It seems to me that the information we so urgently need can come only from large scale controlled clinical experiments such as have been proposed by Meleney of New York. If for instance groups of 50 street accident cases were placed under the observation of a few trained observers and if one group were treated by débridement alone, one by débridement plus Carrel Dakin irrigation or chemotherapy or the local use of the sulfonamides or the Orr Trueta occlusion method it should be possible within a few months to settle the question of how to treat wounds. Such experiments could easily be carried out in the great hospitals of New York, Chicago and Boston supplied as they are with enormous numbers of patients and sheltered from the continuous disruptive ef-

fect of falling bombs. What a grand thing it would be for our soldiers if before the great casualty lists begin the Director General of Medical Services really knew the value of the new methods of treatment and felt himself so strongly supported by experimental and clinical evidence that he could order the adoption of those general principles that offer the greatest hope of success.

I cannot conclude my remarks without thanking you for the high honor you have done me in adding my name to the list of the distinguished surgeons who have delivered the

Oration on Surgery before the American College of Surgeons. I must confess that the word oration at first filled me with misgivings but I find that it really is a word which is used not to cramp the style of the speaker but to do honor to him. Allow me at this moment too, to assure you that the kindly and friendly spirit which has led you in this time of war to select a Canadian as your President is deeply appreciated by myself and my colleagues. The overwhelming evidence of your friendship brings comfort to all Canadians and helps them to face the future with good heart, no matter what that future may hold.

THE PROBLEMS OF SURGERY IN TOTAL WAR

With Special References to Abdominal Injuries

Temporary Surgeon Rear Admiral GORDON GORDON-TAYLOR, C B , O B E , LL D , M A ,
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I PROPOSE to make use of a certain series of abdominal injuries collected from the casualties of this war, and to employ this group of cases as a means of introduction to the consideration of certain clinical phenomena which appear to be novel in this conflict, to certain methods of treatment which are on trial, to the great value of whole blood and the blood substitutes which have been employed on an unprecedented scale in this campaign, and finally to the environment in which many of these patients have been injured or dealt with surgically.

The most prolific cause of injury throughout the centuries has been the warring instinct of mankind. Heretofore, the male has naturally been the sex almost exclusively marked out for this type of lesion, but "total war" makes no sex or age distinctions, and the experience of the Spanish war, which was utilized by Nazi and Fascist merely as a dress rehearsal for the blood bath to be commenced in the autumn of 1939, should have warned mankind of the principles and practice of the aggressors, nay assassins, who are now engaged in endeavouring to institute in Europe what has been inappropriately termed the New Order—surely a most glaring misnomer. Among the more primitive tribes it is almost unknown for the male deliberately to attack or injure the female, and in the animal kingdom it is only on the rarest occasions that the male has made an onslaught upon the female of the species. The wholesale, indiscriminate bombings, involving the lives of countless women, children, babes and sucklings which characterize "total war," forever brand those nations who first introduced and practiced this technique with the stigma of a reputation for diabolical cunning, cruelty, and sheer

blood-lust unknown in any brute or beast.

In ancient times surgeons built up their experience in the workshops of war, and war throughout the ages seems always to have served as a stimulus to advancement in surgical knowledge and craft. It is a little strange that the abdominal surgery of war should have lagged so far behind the operative treatment of similar injuries received under peacetime conditions. Six centuries have rolled past since Henri de Mondeville counselled suture of the colon and affirmed the recovery of some of those who had received wounds of the large intestine, and Ambroise Paré in the sixteenth century, writing of prolapsed and damaged intestine, pointed out that the injuries must be sutured, and evisceration reduced.

The dismal story of the lack of surgical progress in the abdominal surgery of battle, which characterized the centuries up to the period of the last great war, is well known and need hardly be reiterated. The present occasion, however, affords an opportunity for correcting at least one error respecting the history of the abdominal surgery of the war of 25 years ago. If I may be permitted to digress for a moment to the history of the abdominal surgery of that great conflict, the first abdominal operation on the Franco-British front was in fact performed in December of 1914 by the late Captain John Campbell of Liverpool, an alumnus of a famous school of abdominal surgery, the operation was a successful suture of a penetrating wound of the stomach.

The work of Owen Richards, however, really placed the abdominal surgery of warfare on its permanent sound footing. His enthusiasm and enterprise were fittingly crowned by the honor of being the first surgeon on the British Front to save an intestinal wound by means of operative surgery. On March 18, 1915, this surgeon successfully excised six feet of ileum,

perforated in twenty places in some parts the gut was so damaged that two-thirds of its circumference was torn through. The soldier was a Scotch Canadian, who after receiving the injury in a German trench, walked back to his own lines.

The third successful abdominal operation on the British Front in the last great war was performed by Claude Frankau and dealt with a gunshot wound of the colon. Here are recorded three pioneer operations: stomach, small gut colon (Campbell, Richards, Frankau).

No story of the abdominal surgery of war fare would be complete without some reference to Sir Cuthbert Wallace whose enthusiasm and staunch support for his surgeons in the British First Army in the war of 1914-1918 did so much to settle forever the curious controversy upon abatement or intervention for abdominal wounds which had occupied the minds of military surgeons so long. No quixotic fancy made me write a year or two ago. St. Cuthbert must surely be adopted as the patron saint, not only of the luckless stricken in the belly by the missile of an adversary but also of all such surgeons as have a special interest in the abdominal in times of warfare.

After 24½ years of warfare it is perhaps not inopportune to take stock of our experience of the abdominal war injuries of this

total war and to compare and contrast the war surgery of the abdomen of two periods of time separated by a quarter of a century.

The series of 600 operations for abdominal injury in this present review comprises a most motley collection, including abdominal casualties received in naval warfare or admitted into Naval institutions, and civilians damaged by the indiscriminate air bombardments of Britain: there are also included certain Army casualties, represented by the abdominal flotsam and jetsam of the "Dunkirk miracle" and the evacuation of northern France. Still others come from the Royal Air Force and are for the most part those brought down during the epochal Battle of Britain which should be surely termed the Battle over Britain—a nomenclature which perpetuates for all time the prowess of the few to whom so much has been owed by so many. This multifarious

group constitutes a series from which conclusions may justifiably be drawn.

In addition there are also cases of injury to the belly which have been received under circumstances more or less inseparably related to "total warfare" thus for example the "black out" has played no inconsiderable part in determining abdominal damage of this kind. Novel environment has also led to disasters, some of which involve the belly: the spleen has been ruptured through a fall on the stone floor from an air raid shelter bunk (1) by the fall of a warrior on his tin hat or of a sailor upon his gas mask. Catastrophes which befall the individual in peace may also overwhelm him in war and the circumstances of the emergency and the environment of operation may invest both with a panoply of the dramatic.

Abdominal catastrophes consequent upon disease have also been dealt with surgically under "front line conditions": perforated peptic ulcers have been dealt with successfully by operation in hospitals during air raids, and even in the woods adjacent to the Dunkirk beach. Strangulated hernias have been admitted along with air raid casualties during the blitz, and have taken their turn for operation with men and women injured by high explosives.

ABDOMINAL SERIES

Infrequency of operation. In this present conflict the abdominal surgery of war has certainly seemed conspicuous by its infrequency and the apparent paucity of numbers has impressed individual observers whose sphere of surgical activity in the Franco-British Casualty Clearing Zone so odd years ago furnished them with an abundant experience of operative aid for soldiers suffering from wounds in the abdominal area.

In Great Britain, no one hospital no single surgeon, has had so far any vast experience of these cases: they are scattered over innumerable cities, townships, villages, and hamlets throughout the land. The conditions of wounding today are of almost infinite variety and in this "total warfare" the men of the fighting forces and the civilians, the women and children, the aged and the nursing have

suffered injuries to the belly and elsewhere in circumstances as diverse as the missiles and mechanisms of destruction that have damaged, destroyed, or perhaps completely dissipated their bodies

In this "total war" a considerable percentage of the casualties from air bombardment results from crushing force or from the direct or indirect effects of "blast", in crushing injuries the abdomen is less exposed to damage than, for example, the head, shoulders, or limbs, and in lesions due to "blast" the lungs are more vulnerable than the abdomen. Experience has in fact demonstrated that, despite the stout-hearted efforts of rescue squads and the courage and devotion of ambulance drivers in cities, desperate or moribund abdominal cases do not crowd the doorsteps of our hospitals and infirmaries, and it becomes difficult to escape the conclusion that in Britain at any rate abdominal casualties able to repay surgical aid are in truth infrequent

The infrequency of abdominal operations among civilian casualties The following considerations are germane to the discussion

1 The frequency and severity of crush injuries of the trunk, including the abdomen, have been a feature of casualties on the "home front", such injuries are indubitably more mortal than penetrating wounds. Subparietal injuries of the abdomen and its contents played a relatively small part in the abdominal surgery of the last war, this time civilians, women, and children of tender years, and even the unborn babe, are suffering crush-contusions from falling masonry and from burial under collapsed houses and dwellings. Fragments or masses of wood, stone, or metal may be confusedly hurled with devastating force against the abdomen, severe visceral damage or retroperitoneal hemorrhage may be produced by "blast" without any external evidence of injury. The abdominal parietes may suffer along with the subjacent organs, and effusions of blood may be encountered in any of the layers superficial to the peritoneum. Actual rupture of the abdominal musculature along with visceral injury was infrequent in the last war, the blow that ruptured the powerful belly muscles be-

came too spent to damage the intestinal tract. The increase of destructive force nowadays destroys and damages without fine anatomical distinction

2 In towns and villages the most frightful wounds of the belly have been produced by flying glass, abdominal casualties have been eviscerated, or festoons of damaged intestine may be herniated in front and behind, along with other injuries inside the peritoneal cavity. Such are mostly beyond surgical aid.

3 Multiplicity also characterizes the wounds and damage sustained from air bombardment, not only is the mortality raised by concomitant lesions of many viscera, but many, even most of the regions of the body may be simultaneously damaged. The metal and dirt bespattered trunk and limbs in those who had been wounded by high explosives were familiar to surgeons in the last war, but the phenomenon is far more frequent in this conflict, and the severity of the accompanying injuries renders the prognosis in many an abdominal case hopeless.

4 Some of those injured in the belly may also suffer from burns of the body or limbs. This complication of abdominal injury may be encountered in ships or ashore, the prognosis will obviously become far more grave in such cases.

5 The degree of shock encountered among the casualties of this war far transcends that with which surgeons were familiar between 1914 and 1918. Despite the elaborate and highly organized resources of transfusion services, despite the transfusion of many pints of blood or plasma, despite the administration of oxygen, and all the resources of resuscitation therapy, many of the patients with abdominal injuries are past all operative assistance.

6 The clinicopathological phenomena found in men or women exposed to "blast" have been reproduced experimentally by Zuckerman (1940), who has shown that in 40 per cent of experimental animals subjected to "blast" hemorrhagic lesions are found in various abdominal organs. In the realm of human pathology and in experimental work the abdominal viscera appear to be less sensitive to "blast" than are the lungs, and ex-

perimentally in cases in which lesions are present in the belly there are also pulmonary hemorrhages. The special vulnerability of the large intestine to "blast" in the case of the experimental animal is not so marked in the case of men and women the proclivity of the small gut to exhibit lesions due to this casual mechanism is not far inferior to that of the large bowel the stomach is seldom affected. The intestine may exhibit patches of hemorrhage varying from punctiform spots under the serosa to large annular extravasations, and even rupture of the bowel has been known to occur.

The spleen may be torn in persons exposed to "blast" the liver has been bruised or torn, or its right lateral surface may be diversified by lines corresponding to the ribs the kidneys and bladder are less often implicated. Blood clot has been seen in the peritoneum and retroperitoneal hematomas, as well as effusions in the mesentery, are very characteristic. Attention is specially directed to these findings in the abdomen which result from "blast," but once more it should be affirmed that the lungs are especially vulnerable to this mechanism, and that the planes of the head and neck and the nervous system may exhibit similar and perhaps extensive changes. The direct effects of "blast" are experienced close to the explosion only but the many indirect effects may produce death or serious injury at a further distance.

Nevertheless, apart from the actual nature of the abdominal wound, the "time lag" between the hour of wounding and the possibility of expert surgery in a suitable environment obviously plays a most important part in determining the fate of all abdominal casualties not immediately fatal.

The infrequency of abdominal casualties in the forces. The possibilities of the rapid collection of the wounded and their rapid and efficient transport so as to keep the "time lag" within permissible limits must vary with the naval or the military situation. The time factor may be inevitably protracted to the grave disadvantage of the patient by the vastness of the intervening expanse of sea or air.

In army warfare a prolonged time lag should not be so inevitable or capricious save

in circumstances of retirement, since hospitals reserved for the treatment of abdominal and other cases of first urgency should be so mobile that they can be kept within the permissible time lag despite the rapid movements which nowadays characterize war. Alternatively under certain conditions air transport can surely bring surgeon and patient together with the least sacrifice of important hours.

It is manifestly impossible to maintain forward hospitals in an army falling backward especially under conditions of rapid retreat. All patients operated upon before the "break through" must be sent far rearward and for the most recent casualties little more than first aid treatment is possible before evacuation. Such untoward circumstances obviously preclude the possibility of recovery for any large percentage of abdominal cases those that survive owe more to their own physical stamina and stoical fortitude than to the exuberant optimism and enterprise of the surgeon. Abdominal casualties certainly survived the retreat of Gough's Fifth Army in March 1918 and also the more recent Dunkirk evacuation.

In the first clash between the British forces and the enemy across the Channel in May 1940, the military situation precluded the successful performance of abdominal surgery save on a small scale. Cases are known to me of abdominal injuries received during this period of very mobile warfare in which patients were operated upon in France and Flanders, were rapidly embarked at Dunkirk and other French ports and completed their recovery in England. For example, Major W. E. Underwood R.A.M.C. had several successful abdominal cases at this time.

Nowadays, the conveyance of British wounded in hospital ships under the aegis of the Red Cross carried special dangers. Abdominal casualties during transportation across the Channel and the high seas have shared with other injured men the mental torture and perhaps further physical agony from deliberate bombardment of the Red Cross.

In this war the chances of recovery of an abdominal case from such an outrage have been prejudiced still further by the air bom-

bardment of wounded men in the water, a practice which has been freely indulged in by the German and Italian even upon Axis allies, and few that had already been wounded in the belly can have survived

By reason of the environment in which naval casualties are inflicted and the nature of the missiles employed, abdominal wounds are very fatal in ships, although some splendid results have in fact been obtained in men wounded at sea, or even in the sea, during this present conflict. Surgeon-Lieutenant Donald, R N, performed a laparotomy in one of H M Destroyers, when the "naval situation" was such that there was no prospect of transference of the man to a hospital ship or ashore. Unfortunately, the cecum and ascending colon proved to be gravely damaged, with extensive contamination of the peritoneal cavity with liquid fecal material, the man succumbed. An injury to the small bowel might have held out a better hope of recovery.

Immersion in the sea after shipwreck has on occasion been associated with a less familiar abdominal injury, to which Surgeon Commander Rex Williams, R N, has given the name "immersion blast." This will be referred to later in the author's forthcoming Bradshaw Lecture and in Rex Williams' Hunterian Lecture in 1942.

Nowadays there is no safe sanctuary anywhere for the wounded, even in the hospitals and infirmaries of our cities. Wounds from enemy aircraft may even supervene upon medical illness, the Boche never hesitates to hit again when man, woman, or child is down. The destruction of hospital buildings may withdraw from the wounded man the hand stretched out to save him, every hospital in London except two has been hit by indiscriminate air bombardment. A police inspector had been wounded by a bomb splinter which had entered the right flank, presumably damaging some intraperitoneal organ. He was placed upon plasma infusion which rallied him, and the man would without a doubt have been able to be operated upon, unfortunately, the hospital was badly damaged with loss of life to nursing sisters and others, and it became impossible to operate or for a time to evacuate. The man succumbed.

Sex In figures culled from air raid casualties in Great Britain, there is no striking difference in incidence between the sexes. However in one series of abdominal cases in which I have taken particular interest, but *which is a motley collection*, 78 per cent were men, 20 per cent women, and 2 per cent children. Nine of 11 of the infants injured in this series were girls.

Age The youngest victim in this abdominal series to survive an intraperitoneal injury due to enemy action was aged 3 years, this was a subparietal lesion. The next youngest to survive were 7, 8, and 9 years of age, respectively, the mortality in babyhood and early childhood is extreme, although a baby of 10 months recovered from a through-and-through wound of the abdominal wall, which did not implicate the peritoneal cavity.

The following cases perhaps emphasize the horrors of the modern technique of air attack introduced by the totalitarian powers.

A girl of 11 years walked into a hospital, close to which she had been injured by a bomb splinter. She had a penetrating wound of the abdomen situated near the right costal margin and bleeding profusely. At operation, no injury to the gut was found, but there was a severe tear of the right lobe of the liver. The tear was partly sutured and also packed. Despite every form of treatment the wounded girl continued to bleed, and died 24 hours after operation.

The injury from which a little girl of 3 years made a recovery was a subparietal lesion and probably involved an injury to the common bile duct. Her life had been despaired of for several days after she had been rescued from a house in a row which had been completely demolished, she then developed a huge collection of bile in the lower part of the belly, this was drained and convalescence was then straightforward.

A girl of 8 years was an in-patient of a hospital for an operation for cleft palate. During her stay in hospital, the building was badly bombed by Huns, and she received a small perforating wound near the middle line at the level of the third lumbar vertebra. She was hurriedly removed from the damaged building to another institution, and two perforations in the sigmoid flexure were sutured. A proximal colostomy was performed. Recovery took place.

A boy of 9 recovered from a frightful left-sided abdominothoracic injury in which his stomach was protruding from the wound (Alcock).

The youngest living thing known to be destroyed in the maternal womb was a fetus of 6 centimeters! A woman was in an air raid shelter which was destroyed and was thought to present the clinical

picture of blast injury to the lungs. After 48 hours, she succumbed, and at the autopsy the clinical diagnosis was confirmed by the pulmonary changes demonstrable. She had also a large retroperitoneal hematoma, especially marked in the perinephric regions; there was an extensive blood infiltration of the mesentery which had encircled the bowel under its serous coat in several annular patches. The uterine cavity contained some blood, and there was a partial separation of the placenta from the uterine wall. The fetus measured 6 centimeters in length, and showed bruise on its anterior abdominal wall—surely the earliest living thing to receive a blast injury.

After 12 years of age, the prognosis seems to be less dismal.

A girl of 13 was running in the open to an air raid shelter when she was struck by a flying piece of metal. She had a punctured wound of the left para-umbilical region, through which some omentum had been extruded. At the operation (Mr. Donald Thompson) tears were found in the small bowel and transverse colon. The missile was extracted from the rent in the large bowel. The gut injuries were treated by suture. An uninterrupted recovery took place.

Phoebe C., 15 years of age, was admitted to hospital in a state of extreme shock resulting from wounds received from bomb splinters. There were multiple wounds of the back, and a large laceration of the left buttock tracking up between the sacrum and ischium and penetrating the abdominal cavity. Ten hours elapsed before she could be made fit for surgical exploration of the abdomen. She had 7 perforations of the small gut. A large piece of metal was removed. Recovery took place (Mr. Lloyd case).

At the other extreme of life *old age* although naturally increasing risk, does not preclude recovery.

Male 7 years, received penetrating wound of abdomen 3 perforations of small bowel lacerated wounds of scalp and left eyelid, fractures of face, scalp, and hands (Mr. Southam case). This man, despite his years, made surprisingly good convalescence. A plastic operation upon his scalp was successful performed month later.

Annie M. aged 73 recovered from left-sided abdominothoracic wound fortunately no abdominal viscus was injured. The woman, however, had fracture of the fourth rib on the left side and there were lacerations of the right forearm, right breast, and left elbow.

Abdominal injuries of "total war" and pregnancy. It is a ghastly commentary on Nazi *Kultur* that their deeds should have made the record of the following cases possible.

E. S. 30, married, 4 months pregnant, received bomb injury of the abdomen. The severe lacerations of right arm were excised and treated by local chemotherapy. There was also a wound in the right iliac fossa. A glass splinter 3 inches by 1 inch was found lying loose on the cecum; no internal organ was damaged. The abdomen was closed without drainage. It was just too bad that the patient did not miscarry (Major Rodney Smith case).

A married woman 5 months pregnant was injured by the explosion of a bomb close proximity but never attained condition permitting operation. The fragment had entered the left labium major, fractured the left ascending ramus of the pubis, driving a fragment of bone into the bladder; the missile then traversed the pregnant uterus, crossed the cecum, and was finally arrested in the right sacro-iliac articulation. Her daughter aged 7 years, simultaneously received right-sided abdominothoracic wound implicating lung, diaphragm, and liver; the girl recovered.

A woman of years 8 months pregnant, was admitted to Hospital with bomb splinter wound of the left side of the abdomen, through which part of the omentum was protruding. Shock as profound. At operation (Mr. G. H. Balnes case) several perforations of the small intestine were sutured; considerable intraperitoneal hemorrhage was present. A view of the patient's desperate condition the abdomen was closed with through-and-through sutures as hastily as possible. Stillbirth took place the following day. For the first week following operation the poles ranged round so the abdomen as greatly distended. On the tenth day the patient had pulmonary embolism. After this, convalescence smoother although protracted, and she was finally discharged from hospital on the seventeenth day.

A woman, 9 months pregnant, was admitted to hospital with multiple injuries which resulted from bomb explosion. The left buttock was completely destroyed; piece of omentum was hanging out of wound in the belly wall. The patient died without operation.

A woman of about 35 years, 9 months pregnant, was admitted to hospital gravely ill, with a severe fracture of the skull from which brain matter protruded. Shock was extreme; the fetal heart sounds were still audible. It was apparent that the patient was going to die, and the question of cesarean section was mooted. The prospective father and every member of the family had been killed by the same incident, and no operation was performed.

Abdominal injury due to enemy action during parturition. Enemy air raid activity may not only produce abdominal injury in the parturient woman but naturally injuries in other parts of the body may be produced.

The good fortune so far as loss of life is concerned of the well known historical maternity hospitals in London has been remarkable. All have suffered as a result of enemy

action, but no patient has actually been killed within their walls. In another institution the abdominal wall of a patient was ruptured during labor pains, as the result of "blast."

Alice G., aged 36 years, 9 months pregnant multipara, was in the maternity department of a hospital. She complained of labor pains one afternoon, and by evening the pains were strong and frequent. During a severe air raid at night, when several flares lit up the building, she got out of bed and walked along the corridor. At this moment a heavy bomb fell in the hospital grounds about 150 yards from the maternity ward, and all the windows and most of the ceilings in that portion of the hospital were damaged.

The patient collapsed, and examination revealed a loop of transverse colon protruding from a rent in the upper abdomen. This wound was vertical, 4 inches long, and situated over the outer border of the right rectus, the edges were clean cut and bloodless, the bowel was not perforated. There was no evidence of her nightgown having been torn by bomb splinters or glass. A forceps delivery was performed 3 hours after the incident, and a stillborn female child was obtained, the extruded bowel was then replaced. Despite every form of resuscitation the patient died 2 hours later.

Nature of projectile producing injuries. In discussing the nature of the projectiles, it has already been emphasized that many of the injuries received from air bombardment are subparietal or nonpenetrating in character. In the majority of the series of abdominal cases which were selected for special study, a fragment of bombcasing has been the projectile. Certainly in no abdominal case has a large retained fragment of metal been encountered, the largest retained fragment in a patient who recovered was the size of a walnut. In a number of cases the injuries have been produced by bullets. On the whole, these have done well. The increased use of the incendiary bullet adds to destruction and necrosis of tissue produced by burning, in the case of the intestine this may demand resection, where suture would otherwise have sufficed. The recovery rate of those injured by the revolver bullet is flattering to the surgeon.

The destructive effects of flying glass in air bombardments are nowadays familiar to most surgeons. It suffices merely to mention the tragic facial disfigurements in women, the damage or loss of eyes, while in the abdomen coils of intestine may be cut to pieces within

the belly, or may hang out of dreadful gashes in the chest or abdominal wall. A man admitted to hospital wounded by a long spicule of plate glass had the hepatic flexure of the colon and a coil of small gut completely divided, his right kidney was cut in sunder, and the continuity of the renal vessels at the hilum, the man died despite operation.

Small puncture wounds produced by glass may betray catastrophic lesions within. A blood stain on a woman's night dress revealed a small punctured wound in the epigastrium. On wiping away a clot which had temporarily sealed the small wound, a column of blood a foot high spurted upward. A splinter of glass of the size of the index finger was withdrawn from the liver. The patient succumbed.

Sometimes visceral injury produced by glass is less severe, and lesions of the bowel have been successfully treated by surgery. Sometimes, there may even be peritoneal penetration, without visceral damage.

A patient may be wounded by glass and bomb splinter, for example, a man had numerous punctured wounds all over the body due to glass, one tiny puncture was situated just below the left costal margin. There was no shock, but lower abdominal pain and infinite tenderness below the umbilicus.

Operation was performed by Mr. Meyrick Thomas and Mr. Desmond Cooper. After excision of the wound, when the track was followed inward, it appeared definitely to end at the level of the external oblique aponeurosis. However, when this was incised the track was found to pass through the internal oblique and transversalis, and a tiny puncture wound in the peritoneum. The peritoneal cavity contained a quantity of blood, small wounds in the anterior and posterior walls of the stomach were sutured, a small retroperitoneal hematoma was found, and a spurting artery in the position of the coronary artery where it was just leaving the posterior abdominal wall to enter the lesser omentum. Subsequent x-ray examination showed a small dense fragment low down at the level of the lumbosacral junction. Recovery took place.

A man received a double injury under unusual circumstances. When milking a cow, he was hit in the upper part of the buttock by a bomb splinter and gored in the thigh by the animal. He was found to have two perforations of the small bowel, which were sutured, the cecum was "grooved," but not perforated. There was a wound of the right anterolateral surface of the bladder, and the fragment was found in the

cavities. The thigh wound inflicted by the cow was very extensive. The man made a good recovery (Mr M. D. Shepherd's case).

In addition to glass fragments, debris, stones, and mud other foreign bodies may be met along with bomb fragments.

A man standing in the street received abdominal injuries from a bomb splinter: the wound of entry was situated under the left costal margin, the wound of exit in the lumbar region; the left of the spine. Operation revealed a complete severance of the transverse colon, a bomb splinter and penaeus (?) were removed from the track. Unfortunately the man died.

Viscera may be damaged by in-driven bone fragments, although the missile itself does not penetrate the peritoneal cavity. This has happened especially with fractures of the innominate bone, sacrum, ribs, etc.

Hollow viscera have been punctured by metal fragments which have not penetrated the peritoneal cavity. Cases of bowel injury by indirect violence were reported by Owen Richards, Sir John Fraser and others in the last great war. One such case had both recti abdominis almost completely divided by a through and through wound which was explored and the peritoneum was found intact. Nevertheless, the man succumbed and 3 lacerations in the small intestine were present. The injured piece of bowel lay immediately underneath the wound of the abdominal parietes. Similar cases have been met with in this war for example:

E. N. female aged 43 years, was admitted to hospital half an hour after being wounded by high explosive bomb. On admission, shock was found to be only mild, there was deep laceration of the right groin just below Poupert's ligament, which appeared to involve the tissues behind the ligament and also the extraperitoneal structures of the right iliac fossa. There was no wound of the abdominal wall itself and no evidence of intra-abdominal lesion. Three hours later tenderness and rigidity had developed on the right side of the abdomen and laparotomy was now clearly indicated. At operation (Mr Wase) it was definitely established that no communication existed between the wound in the groin and the pelvic cavity. Nevertheless 3 perforations of the lower ileum were found to be present.

There are only two bayonet wounds in this series.

An enemy agent, during the Dunkirk evacuation, was bayoneted through the right lower chest in the

black-out. There was lacerated omentum of entry over the ninth right rib, which was fractured; the wound of exit was situated in the right hypochondrium anteriorly. There was considerable abdominal tenderness, but apart from the excision of the wounds of entry and exit, the man was treated on conservative lines. He recovered (Major A. S. Telford's case).

F. P. (Mr J. S. Horn's case) aged 24 years, a soldier, was sent to hospital with the history that he had fallen on his bayonet while in practice. The bayonet had been removed from the left ischio-rectal fossa where it had entered, and a stitch had been put in the skin as the bleeding had been profuse. There was a small exit wound in the left subcostal region. He was very shocked and given a pint of citrated plasma, followed by a drip transfusion which was continued during the operation. At laparotomy the spleen and left kidney were found to be uninjured, but there was a small hole leading from the peritoneal cavity into the base of the bladder. The bladder was therefore opened, and an attempt was made to suture it, after which both the bladder and the peritoneal cavity were closed with drainage. The wound in the buttock was sprayed with sulfadiazole powder and drained, as was also the wound in the side. After somewhat stormy convalescence, he recovered.

Immunity of viscera in penetrating injuries of the abdomen. The occasional immunity of viscera in penetrating wounds of the abdomen first suggested in the South African War confirmed in the last great war has again been re-established.

Spontaneous recovery from indubitable wounds of the hollow viscera which was demonstrated by Makins, Cuthbert Wallace, Green-Armytage, Gordon Bell among British surgeons in the last great war has been confirmed by the experience of today.

The buttock wound. In 59.6 per cent of penetrating wounds of the belly the wound of entry is anterior. In 40.4 per cent, the wound of entry is on the posterior aspect of the body. In half of these (20 per cent of total) the wound is in the buttock. The dangers of overlooking the buttock wound were stressed in the last war: the great frequency with which this constitutes the portal to the peritoneum emphasizes the necessity of completely stripping the patient and the most thorough examination of the whole body.

J. S. (Mr Greening's case) aged 3 years, dactylitis, had been treated intermittently for syphilis since 1937. In the beginning of 1944 her Wassermann

was ++, and she was under treatment when she was wounded by a fragment of bomb. The patient, in addition to intravenous injections, had also received a very large number of injections of bismuth in the buttocks. On January 11, 1941, it was the left buttock that the missile entered, passing upward and across the abdomen to the right iliac fossa. She made a satisfactory recovery from an operation which comprised a resection of 6 inches of ileum and the suture of two other perforations of this portion of bowel as well as the suture of a wound in the bladder. Her courage and pluck were such as to stimulate her to return to the "West End of London" 4 weeks after her operation. She had discharged herself from hospital against surgical advice. Subsequently, she required treatment for the removal of sequestra from the ischium and for an infection of her bladder with *Bacillus coli* and *Bacillus proteus*.

Direction of missile track. Wounds which track across the abdomen from side to side enjoy a more sinister reputation than those whose direction is anteroposterior.

The case of a very successful result is recorded as follows:

A member of the Home Guard (Mr I. H. Bentley's case) was accidentally shot through the abdomen by a rifle bullet, sustaining 13 perforations in small intestine. The abdomen was opened 4 hours after the injury, and after the intravenous administration of 2 pints of blood and was found to be completely filled with blood. The bullet had splintered the ilium and was lodged in the left iliacus; the hemorrhage had largely proceeded from the laceration of the pelvic mesocolon. The continuity of the small bowel after resection of 4 feet of damaged jejunum was effected by an end-to-end junction. An uninterrupted recovery ensued.

The vertical wound track had also a bad reputation in the last war, many specimens in the former collection at the Royal College of Surgeons illustrating the truth of this statement.

A case with a successful outcome occurs in this present series.

A woman, Ethel K., received a penetrating wound of the left buttock. An x-ray film showed the presence of the fragment high up under the cupola of the diaphragm. There was a quantity of blood in the pelvis, and there was much retroperitoneal bruising, and hemorrhage in the left iliac fossa. Two perforations of the jejunum were sutured. The patient made a good recovery.

The large wound involving one of the cavities of the body is nearly always fatal, the man with a large wound of the abdomen or a wide loss of the abdominal wall seldom recovers.

A patient was admitted to hospital with an extensive abdominothoracic injury, including a large

perforating wound, 8 by 4 inches in the left lower chest and left hypochondrium, associated with a pneumothorax, a lacerated diaphragm, and a perforation of the splenic flexure of the colon; he lived 5 days after operation, dying of pneumonia. The lower 6 ribs were fractured on the left side, and the fractures were implicated in the huge wound. There was also a second wound of the thoracic wall 3 by 3 inches which involved only skin and muscle. The capsule of a sclerotic spleen was torn, but had not occasioned hemorrhage, no treatment for this was needed. The torn diaphragm was sutured to the parietes with improvement in respiration and general condition. The dimensions of the wound and loss of tissue precluded its complete closure.

A man admitted to hospital after injury from a bomb had the anterior abdominal wall, including the peritoneum, completely torn away. Numerous pieces of rubble of varying size covered the presenting intestinal coils. There was a complete rupture of the transverse colon and several perforations of the jejunum. Mr Desmond Cooper, working at top speed, brought the two ends of the damaged colon to the surface, sutured the perforations of the small gut and made a gallant attempt to close as much as possible of the anterior abdominal hiatus. Despite the fact that the operation was completed in 15 minutes and all the resources of transfusion therapy employed, the patient succumbed.

This dismal story might be told and re-told almost indefinitely, nevertheless, some wonderful recoveries have taken place and constitute veritable triumphs of surgical skill.

Mr Arnold Alcock's case is perhaps specially remarkable, inasmuch as the boy was only 9 years of age.

A boy of 9 years was admitted to hospital with a large wound 8 inches long in the lower part of the left thorax, fifth, sixth, seventh, eighth, and ninth ribs were splintered, and there was a tear in the diaphragm 4 inches long. From this traumatic chasm the stomach protruded; there was a small puncture wound on the lesser curvature which was fortunately not large enough to permit the contents of the replete viscus to flood the thoracic and abdominal cavities. There were also several incomplete tears of the gastric wall, produced by the fractured ribs. The lung appeared undamaged. The perforation in the stomach was enlarged, and a mass of undigested vegetables emptied from its cavity; the gastric wound was sutured. After a thorough excision of the wound, the diaphragm was sutured, and the thoracic wall closed, a Malecot catheter was introduced into the pleura through a separate incision posteriorly. After an anxious week, the patient's progress was maintained and he made a good recovery.

A seaman (Mr John A. McLauchlan's case), of 40 years of age was admitted to hospital for injuries due to a bomb fragment. There was a large wound, 8

itches long, over the eighth, ninth, and tenth ribs on the right side just above the costal margin. The seventh to eleventh ribs inclusive were fractured and at 11 p.m. The pleural cavity was opened, the diaphragm torn, the upper surface of the liver lacerated, and the upper pole of the right kidney punctured. The wound was excised, the liver sutured, the diaphragm repacked. The jagged and comminuted ends of the broken ribs were removed, and the diaphragm was attached to the thoracic wall above the rent. The chest was closed; livers. Recovery took place.

Nonpenetrating or subparietal abdominal injuries. Careful postmortem investigation disproves the belief that fatal casualties without external wound are frequently abdominal injuries. In only about 10 per cent of all fatal casualties in one series of cases could death be attributed to an abdominal lesion; a primary blast effect could only be impugned as the causal mechanism in a tiny fraction of these. Most of the abdominal lesions among these fatal cases were caused by collapse of buildings, and crushing injuries or by blows upon the belly by flying missiles or portions of collapsing buildings. Injury to the spleen was the most frequent form of visceral damage to occasion a fatal issue but the liver, kidney, duodenum, and small bowel were also damaged in mortal injuries and in 1 case hemorrhage from the uterine vessels caused a fatal hemoperitoneum.

In casualties due to air bombardment of cities, many of the injuries are not the primary effects of the explosion, i.e. are not produced by splinters or the direct impact of a blast wave. Perhaps most casualties are due to the secondary and tertiary effects of the bomb detonation.

Those effects are said to be secondary when injuries are due to the patient being bowled over by the blast wave or as a result of a splinter wound and thus injuring himself (Zuckerman). Tertiary effects are due to the impact of dislodged masonry fragments

causal mechanisms operating in cases of parietal abdominal injury met with in war.

A patient, woman of 33 years, was blown blast across a room against a steel partition, holding then collapsed on her crushing her side down into a crouching position. Release effected in about half an hour after the incident. Contusion of the lung, possibly due to blast diagnosed. A view of the thoracic condition, abdomen was most wisely opened under local anesthesia. The pelvic hematoma was found to be stripped the peritoneum half way up the abdomen. The anterior wall of the bladder, great blood supply drainage was instituted, pure blood previously been obtained on catheterization. A valvulus was complicated by consolidation of left lung, paralytic ileus and by temporary ileus. Ultimate recovery was complete (Miss Lord case).

The abdomen of another patient has been severely contused by flying bricks from a direct hit by bomb on a street air raid shelter. She had perforations of the jejunum, which were successfully sutured, a hematoma of the mesentery was also excised.

Under similar circumstances, a woman had ovarian cyst ruptured, 4 pints of blood-stained fluid were evacuated from the abdominal cavity and sac of the torn tumor was removed. Recovery took place.

The collapse of the roof of a house which had craved direct hit produced a complete division of the jejunum in a man of 6 who recovered after end-to-end suture of the bowel.

A crush injury due to collapse of wall produced separation of the pubic bones at the symphysis, fracture of the humerus posteriorly but had also the mesentery of the terminal small gut. The laceration was transverse and two arteries were still spouting at the time of operation. The bowel was viable and made good recovery.

Winifred C. aged 25 years, was admitted to hospital for injuries sustained when her bonnet collapsed upon her and a piece of concrete fell across her abdomen. Her injuries included multiple abrasions on the face, 3 deep wounds of the scalp extending down to the bone, deep wound of the medial aspect of the left knee which did not implicate the joint and a wound over the left olecranon. An indefinite

tion of mines at sea, the exact mechanism has not always been evident, in some cases decks have actually fallen in and exerted a crushing effect

A man was admitted from a "mined" ship, the galley in which he worked caved in upon him. In addition to burns of both hands, he had a diastasis of the symphysis pubis, and a fracture of ascending and descending pubic rami. A small extraperitoneal rupture of the bladder was present, and there was urinary extravasation into the Cave of Retzius. Post-operative ileus complicated his convalescence, but he ultimately made a good recovery (Mr W E C Wynne's case).

Another man admitted from a mined ship had a fracture dislocation of the knee and evidence of abdominal injury. He had been in the water some time before being picked up. There was gross bruising of the transverse mesocolon, and also numerous petechiae on the bowel wall. The right kidney was contused. The limb required amputation, but the man recovered (Mr W E C Wynne's case).

Some abdominal injuries have definitely appeared to have been caused by blast. Mr D H Patey had 1 case, in which a man running away from a bomb was exposed to the blast wave. There was no sign of any external injury and no history of any blow from any fragment of timber or masonry. His mesocolon was torn in the vicinity of the splenic flexure of the colon with resultant hemorrhage.

Another case was that of an intramural thrombosis of the blood vessels of the right side of colon (Mr Blacon Yates' case).

P H, male, aged 38 years, was admitted to hospital in a state of extreme shock, he had been in close proximity to a detonating bomb, although the exact distance which separated him from the missile was never actually determined. Abdominal pain was not marked, 1,000 cubic centimeters of plasma was first administered by drip transfusion, then a pint of blood, followed by 600 cubic centimeters of 5 per cent glucose saline. His general condition slowly improved, 24 hours after admission the abdominal pain became more severe, especially on the left side of the abdomen. At 30 hours, clinical evidence of diffuse peritonitis was apparent, and laparotomy was performed. The only visceral lesion discovered was gangrene of the anterior surface of the cecum and proximal 2 inches of the ascending colon. The condition appeared to be due to intramural thrombosis of the vessels of the bowel wall, the vessels of the mesentery were quite normal.

W J L, under the care of Mr H Donovan, succumbed from subparietal injury, this case definitely

appears to be one of blast injury to the abdomen. The thoracic pathological findings confirmed the nature of the causative mechanism, the liver showed intrahepatic tears and hemorrhage, and a large subcapsular hematoma. The right suprarenal also contained a hematoma. The inferior pole of the cecum contained a small hematoma, the ascending and transverse colon exhibited marked bruising. There was a tear in the seromuscular tunics of the transverse colon.

In Mr Hamilton Barclay's case, a man was in the open when a high explosive bomb detonated in close proximity to him. He had not been struck by any fragment, nor fallen on his belly. There was a large hematoma of the great omentum, and a certain degree of hemoperitoneum. An extensive retroperitoneal hematoma was present, and a horizontal rupture of the abdominal wall, the tear extending from the peritoneum through the muscular wall of the parietes to the skin, which was intact.

In respect to injuries due to blast, it must be remembered that "blast injury of the lungs" by reason of the abdominal pain produced may suggest the diagnosis of an abdominal lesion. Some of these patients have rigid abdominal walls, possibly the pain and rigidity may be caused by hemorrhage in the thoracic intercostal spaces.

X-ray examination of the chest should enable a diagnosis to be made of pulmonary concussion, and the physical signs in the chest, especially the bulging of the chest wall, should prevent an unnecessary laparotomy.

Nonpenetrating or subparietal injuries of the abdominal viscera may occur under circumstances less directly connected with the destructive mechanisms and missiles of total warfare. The "black-out" is a fruitful source of such mishaps, their name is legion and their variety infinite.

The subject of "*Immersion Blast*" is being dealt with by Surgeon-Commander Rex Williams R N in his Hunterian Lecture in 1942, and also by the writer in his Bradshaw Lecture for 1942.

Lesions of the stomach in "total" warfare. This war has added little to our knowledge of penetrating wounds of the stomach. Operations for wounds of the stomach have given a recovery rate of 60 per cent in this series from the present war, this is a marked advance from 36.3 per cent in the last war (Cuthbert Wallace). Wounds are of infinite

variety depending on the size, shape and velocity of the missile the direction of its flight the state of the stomach in respect to repletion or vacuity etc. In some cases, the wounds have been wide and gaping in a wounded man coming under the care of Mr Blacow 3 days the wound in the stomach was 4 inches long and the mucous membrane was extensively everted In another patient operated upon by Surgeon Lieutenant-Commander B C Murless, R.N.V.R. the gastric rent extended from the esophageal opening to the greater curvature. In a successful case of Mr J Scholefield, the stomach wound was 3 inches long

Eversion of the inner tunics of the stomach wall was said in the last war to be most marked at the curvatures and in wounds of considerable dimensions. In the present series of cases under review no mention is made of the note of exclamation wound, to which Sir Cuthbert Wallace drew attention. In several of the recent cases, severe hemorrhage has taken place into the celomic cavity

There is one condition of the stomach which has impressed by the striking frequency of its occurrence in this war—*acute dilatation of the stomach*. Not only has this phenomenon been a concomitant of penetrating injury of the abdomen but it has also proved an undeniable and sometimes intractable sequel of operations undertaken to repair the damage inflicted by the detonation of bombs from enemy aircraft.

H. H., male aged 35 years, was injured by bomb fragment there were multiple flesh wounds of left thigh, buttocks and epigastrium. An exploratory laparotomy revealed no visceral injury the patient had to be prematurely evacuated to base hospital, where he arrived very ill and shocked and was found to be suffering from acute dilatation of the stomach. This was relieved by continuous suction drainage intravenous infusion promoted satisfactory convalescence

A girl of 17 was in the kitchen of a house which received direct hit from a bomb the house came down on top of her father (who died shortly after admission to Hospital) her mother and two day old baby (who both recovered) and herself. She was moderately shocked extensive bruising of the pelvic region and chest was present. Radiography showed fractures of the ischium and pubes on the right side and of both rami of the pubis on the left side. The radiologist commented upon the condition of

acute dilatation of the stomach. At operation, an extraperitoneal rupture of the urinary bladder was found. Despite suction drainage of the stomach the gastric condition never ameliorated, and she succumbed 66 hours after operation.

Surgeon-Commander Rex Williams, R.N. In private communication mentions a case of penetrating wound of the abdomen that died on the sixth day from acute dilatation of the stomach, despite every effort to control the complication

Acute dilatation of the stomach may supervene at a still later date after wounding, may defy all treatment, and may determine a fatal ending

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Mr N R. Barrett and Mr Price-Thomas have drawn my attention to the sudden acute dilatation of the stomach which frequently takes place in contusions of the chest

Perforation of peptic ulcer The circumstances under which perforation of a peptic ulcer may occur and operation be undertaken for its repair may invest a mundane occurrence and a banal surgical procedure with a dramatic color

Several ulcers are known to have perforated during air raids on the country and several have been operated upon during the "blitz"

A male patient, T D, perforated a duodenal ulcer during progress of an air raid on Merseyside and was removed to Hospital, operation for its repair was in progress, when the hospital got a direct hit, putting the operating theater department completely out of action. The laparotomy wound was temporarily closed, the patient removed to another institution, where the operation was completed by the resident surgical officer, the man recovered.

Another patient was being operated upon for a perforated duodenal ulcer when the detonation of a mine in close proximity brought the roof of the theater with superjacent sandbags down upon patient and those engaged in the operative relief of his condition. The emergency lighting system fortunately proved itself worthy of its name, and the operation could be continued. The debris, glass, dust, and sand were assiduously removed from the abdominal cavity, the perforation was sutured. The man made a good recovery, his only complaint being of "the dust in his eyes."

A rear-gunner in a Blenheim bomber perforated a duodenal ulcer over Dunkirk, he thought that he had been wounded by "Flak."¹ On the return of the aircraft he was admitted to hospital as a casualty from enemy action, no wound was discoverable. The real condition was then diagnosed, and the patient successfully operated upon by Group Captain Stanford Cade.

I have knowledge of at least 3 ulcers which perforated during the "Dunkirk miracle," in which recovery took place. The number of loyal stout-hearted men who, weary though they were, contributed in diverse fashions to the ultimate recovery of their comrades cannot have been inconsiderable.

Intestinal injuries The recovery rate of intestinal injuries due to enemy action which are operable has surprised me. Of the patients with small bowel lesions 47 per cent have recovered, and 40 per cent of those with large gut lacerations. Suture carries a lower mortality than resection for wounds of the small intestine and should be preferred whenever possible. This doctrine, as the perusal of case records clearly demonstrates, is firmly inculcated in the minds of British surgeons, in the Spanish War operators seemed disposed to resect when the ileum was the segment of bowel damaged and to suture when the jejunum was involved. The type of resection

and anastomosis employed is a matter of individual choice and experience, and is not a fashion which varies from war to war. My predilection led me to use end-to-end suture in the last war in every intestinal injury in which bowel resection was indicated.

The specter of the "dangerous mesenteric angle" was permanently robbed of its terrors in the light of the experience of the last war, since no case was found to demonstrate that fatal peritonitis was ever due to leakage at that angle. Peritonitis was invariably due to infection introduced with the missile at the time of wounding or subsequently from the injured gastrointestinal tract, especially the large gut, and was in no way causally related to the technique of bowel anastomosis. Lengthy resections of small intestine imply severe and widespread wounding, the ablation of short segments of gut is therefore more promising. Nevertheless, the removal of 6 feet of small intestine and the cobbling of other injuries proved successful in the last war (Owen Richards, Gordon Bell, Gordon-Taylor), in this war Surgeon Commander T N D'Arcy, R N, saved a 6-foot resection of small bowel severely damaged and burned by a phosphorus bullet, F H Bentley, a 4-foot resection.

I have sometimes been credited with the advocacy of resection as opposed to suture in cases of injuries to the colon produced by enemy action. This is far removed from the truth. There can be no doubt about the place of suture in most intraperitoneal colon wounds, and also about the indication for suture in conjunction with efficient drainage of the neighboring area in many extraperitoneal injuries when this technique offers a reasonable prospect of success, suture, local chemotherapy, and drainage of the damaged area may be combined with proximal colostomy in cases in which grave infection is feared.

Colostomy sometimes proved valuable in the last great war as a prophylactic measure against infection of the lethal retroperitoneal tissues, if this operation is performed, it should be practiced early, before infection has secured a firm hold of the region. Sulfonamide therapy, local and oral, has already proved a valuable adjuvant to surgery for patients with damaged large intestine, and its routine use prophylac-

¹A fragment of anti-aircraft shell.

variety depending on the size shape and velocity of the missile the direction of its flight the state of the stomach in respect to repletion or vacuity etc. In some cases the wounds have been wide and gaping. In a wounded man coming under the care of Mr Blacow Yates the wound in the stomach was 4 inches long and the mucous membrane was extensively everted. In another patient, operated upon by Surgeon Lieutenant-Commander B. C. Murless, R.N.V.R., the gastric rent extended from the esophageal opening to the greater curvature. In a successful case of Mr J. Scholefield the stomach wound was 3 inches long.

Eversion of the inner tunics of the stomach wall was said in the last war to be most marked at the curvatures and in wounds of considerable dimensions. In the present series of cases under review no mention is made of the "note of exclamation" wound, to which Sir Cuthbert Wallace drew attention. In several of the recent cases, severe hemorrhage has taken place into the celomic cavity.

There is one condition of the stomach which has impressed by the striking frequency of its occurrence in this war—*acute dilatation of the stomach*. Not only has this phenomenon been a concomitant of penetrating injury of the abdomen, but it has also proved an undesirable and sometimes intractable sequel of operations undertaken to repair the damage inflicted by the detonation of bombs from enemy aircraft.

H. H. male aged 35 years was injured by bomb fragments there were multiple flesh wounds of left thigh buttocks, and epigastrium. An exploratory laparotomy revealed no visceral injury the patient had to be prematurely evacuated to base hospital, where he arrived very ill and shocked and was found to be suffering from acute dilatation of the stomach. This was relieved by continuous suction drainage. Intravenous infusion promoted satisfactory convalescence.

A girl of 17 was in the kitchen of a house which received direct hit from a bomb, the house came down on top of her father (who died shortly after admission to Hospital) her mother and 10 day old baby (who both recovered) and herself. She was moderately shocked, extensive bruising of the pubic region and chest as present. Radiography showed fractures of the ischium and pubes on the right side and of both rami of the pubis on the left side. The radiologist commented upon the condition of

acute dilatation of the stomach. At operation, an extraperitoneal rupture of the urinary bladder was found. Despite suction drainage of the stomach the gastric condition never ameliorated, and she succumbed 96 hours after operation.

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¹A fragment of anti aircraft shell.

tically is to be recommended. I foresee nothing likely to alter the indications for resection of the injured colon which I have ventured to promulgate on more than one occasion: (a) the cecum or colon is in a state of infarction; (b) there is extensive separation of the bowel from its mesocolon or vascular supply, especially if the mesocolon is also the site of a hematoma or is actively bleeding; (c) the vitality of the bowel is extinguished by a large piece of metal or other fragment buried with the cyclopean force of modern high explosive; (d) the wound of the large intestine is of such magnitude, or the surgical approach to the part of the colon damaged is associated with such difficulty as to suggest the formation of an artificial anus as a surgical *pis aller*.

I only know of two successful exteriorization operations for injuries of the large bowel in this war.

In the traumatic colonic lesions of war it is preferable to complete the resection quickly by the form of anastomosis with which the operator is most familiar. The addition of a prophylactic or of a temporary intraperitoneal colostomy is a useful and perhaps life-saving expedient.

Multiple resections of bowel. Multiple resections of bowel were often successfully performed by surgeons before the last war for various pathological conditions unconnected with traumatism. During the war of 1914-1918 plunsegmental resections for injury aroused grave forebodings in the minds of operators, and various recommendations were made in order to obviate the necessity of removing more than one length of damaged intestine. Nevertheless, I had 11 successful cases of double resection, which represented a 50 per cent recovery rate in the patients submitted to this operation at my hands. No case of a successful triple resection for gunshot injury of the bowel was known to me in the last war, although W. A. Campbell had a triple resection with death from a chest complication when success appeared to be within his grasp. During the last 25 years successful multiple resections of intestine are of almost everyday occurrence, and I myself have had numberless cases of double and even of triple ablations. I recall the case of 1 patient who actually sur-

vived the removal of 7 segments of bowel for a complex and complicated carcinoma of the colon!

During the present War Meyrick Thomas has brilliantly and successfully performed a quadruple resection of small intestine damaged by a "tommy-gun" at close range.

T. L. was shot in the abdomen about 36 hours previous to admission to hospital. There was a small wound of entry about 1 inch below the umbilicus with about 1 inch of bleeding omentum protruding. At operation a part from several simple sutures of damaged gut, 4 resections of shredded length of ileum about 1 to 2 inches long were found necessary. End-to-end union was employed in each case. The distance separating the various anastomoses varied from 12 to 18 inches. Four wounds of the bladder were found, but the condition of the patient did not permit of anything more than a temporary suprapubic drain. He made a good recovery.

Protrusion of the abdominal viscera. Prolapse of the omentum has a diagnostic rather than a prognostic value; the prognosis depends upon the associated visceral damage rather than upon the fact of damage or extrusion of the omentum itself.

Hernia of the bowel resulting from enemy action varies from complete evisceration to the protrusion of one or two segments of intestine. Over 20 years ago cases with extrusion of gut were accounted bad surgical risks; nevertheless, Owen Richards' successful pioneer operation was performed upon a soldier with extruded and damaged intestine. Among others, the writer had several successful cases of suture or resection of prolapsed bowel. From the material now under review the recovery rate from operation for prolapsed and nonperforated small intestine is about 50 per cent, the mortality being mainly determined by concomitant damage, but when the small gut is not only extruded but also injured the mortality is about 80 per cent.

In cases of prolapse of the large bowel the prognosis is very grave, although several remarkable recoveries have been effected by skilful and courageous surgery. For example, Mr. F. J. S. Heaney successfully operated upon a man of 26 who was injured in the street by a bomb splinter. On his admission to hospital the large intestine extruding feces was found to be prolapsed through a large rent in

the left loin After resuscitation with 2 pints of plasma, he was operated upon 3 hours after admission

The wound was thoroughly excised, the damaged prolapsed descending colon was removed, and a side-to-side junction effected between the transverse and the pelvic colon The peritoneum was completely closed, but the posterior portion of the flank incision was left open A prophylactic temporary cecostomy was performed A fairly normal convalescence was established

In view of the grave prognosis which attends *prolapsed and damaged bowel*, the following cases are noteworthy

A patient (Mr O V Lloyd-Davies' case) was admitted to hospital with a huge lacerated wound of the lower right quadrant of the anterior abdominal wall, and most of his bowel lying in his trousers Shock was profound, but the man was conscious The usual methods of resuscitation were utilized, including a blood transfusion, the clothing was slit up, and the prolapsed bowel merely covered with a warm saline pack The abdomen and the extruded gut were covered with stone fragments, mud, mortar, etc., the 2 lacerations of the ileum were repaired by suture The wound in the abdominal wall was widely excised, the extent of tissue loss was now alarmingly evident, and much ingenuity was required to close the peritoneal and muscular gap The skill of the surgeon and the scientific postoperative measures contributed to the successful issue (a) Continuous stomach suction was continued until normal peristalsis was heard all over, and until there was no distention and the bowels were open normally (b) Continuous intravenous drip (1 bottle of normal saline in proportion to 4 bottles of isotonic glucose, if good cloud of urinary chlorides, glucose increased and vice versa) This was continued for 13 days As much as 15 pints per 24 hours had to be given at first to keep pace with the measured and estimated fluid loss Peristalsis gradually became normal, low pitched and present all over the abdomen, fluid was now passing through from the stomach, careful dosage of prostigmine, 1 cubic centimeter intravenously, and later small doses of Epsom salts started normal bowel action The wound was septic, but held together astonishingly Three months later the man was readmitted to hospital with signs of intestinal obstruction A straight x-ray picture showed numerous small gut fluid levels all over the abdomen At operation, numerous adhesions were found, most marked in connection with the lower small intestine and in the ileocecal region Multiple adhesions were divided, a small perforation occurred and was sutured After treatment was the same as before Recovery was complete and he is doing moderately heavy work, wearing a canvas belt

A member of a bomb disposal squad (Mr Geoffrey Parker's case) was standing in the open, about 10 yards away from the bomb, when it exploded His clothes were partly torn off, and his intestines were found "lying in the grass" On admission to hospital, he had a large wound in the right iliac fossa, about 4 inches diameter in all directions A field dressing somewhat inadequately covered the 3 feet of prolapsed ileum One loop of ileum had 2 large rents, almost completely dividing the bowel, the mesentery of this portion of the bowel was also damaged A limited resection of small gut was performed The parietal peritoneum was also extensively torn up, and blood had exposed the extraperitoneal aspect of the bladder, and had tracked through the femoral canal into the thigh and along the spermatic cord The blood was found to come from the horizontal ramus of the pubis, in which was impaled a small piece of bomb casing The man made a good recovery

Wounds of the duodenum The Spanish War confirmed the sinister reputation of wounds of the duodenum and pancreas which had been established in the great war of 1914-1918 The number of cases of injury to the duodenum at present available is too small for any reliable conclusions to be drawn as to the fatality of these wounds, it may be said, however, that successful operations have been performed for duodenal injuries in this present war (Rex Williams, Hedley Atkins, Henry R. Thompson and T J Cobbe)

Driver B (Mr Hedley Atkins' case) was wounded in the loin by a machine gun bullet while lying face downwards on the deck of one of H M Destroyers which was transporting him from Dunkirk to England The wound of entry was about half an inch in diameter and situated close to the spine, the track thence passed forwards and to the right between the first and second lumbar transverse processes When seen 4 hours after wounding, his general condition was good He had vomited once or twice, his upper abdomen was rigid, but peristaltic sounds were normal The wound in the loin was first dealt with, and next the abdomen was opened by a high right paramedian incision The peritoneal cavity was full of blood, there was a perforation of the anterior wall of the second part of the duodenum, and also on the posterior surface of the liver, from this latter blood was oozing freely The bullet had obviously skirted the medial border of the superior pole of the right kidney and had damaged both walls of the duodenum The wound of the anterior wall of the duodenum was sutured, the peritoneal cavity cleared of blood by suction, and the rent in the liver plugged with gauze Some discharge of duodenal contents took place from the wound in the loin, but this ceased after a few days and the man made a good recovery

Rare as are successful operations for duodenal injuries, Henry R. Thompson has actually two to his credit

Jack S. a boy of 16, was hit in the street by a fragment of bomb. On admission to hospital, shock was severe, there was cyanosis of lips and cheeks. He complained of pain in the pit of the stomach, and had vomited once. There was retrograde amnesia. A puncture wound was present, centimeter in diameter and situated $1\frac{3}{4}$ inches internal to and just above the left anterior superior iliac spine. There was marked tenderness over the ascending colon and absence of intestinal sounds. There was a graze over the right costal margin and a small wound on the flexor aspect of the left forearm. At operation a perforation of the duodenum near the pyloroduodenal junction as closed by suture and similar perforation of the anterior wall of the stomach was treated in a similar fashion. Despite subsequent right basal pneumonia the patient made good recovery. A fragment of metal was seen on x-ray examination to be still present in the right upper abdominal quadrant probably in the liver.

The second man, sleeping in bed on his back when, as a result of near miss bomb was shaken in the small hours of the morning by what appeared to be a severe blow on the abdomen the injury may have been due to blast, or some fragment of the bomb may have hit his abdomen, although there is no bruise or abrasion to indicate such mechanism. On admission to hospital, the patient as in considerable abdominal pain the pulse rate was 80, he was tender and rigid in the upper right abdominal quadrant. The man was kept under close observation, and after 3 hours, although there was no change in the pulse rate or in its volume, the tenderness and rigidity now involved the whole of the right side of the abdomen. Operation was performed 6 hours after the injury. A large subserous hematoma was found, which had spread over the duodenum from the pyloric end of the stomach and had infiltrated into the layers of the transverse mesocolon. The peritoneum over the duodenum was found to be ruptured at the junction of the first and second portions. The rupture of the bowel was not quite complete about $\frac{1}{4}$ centimeter gut still was still intact. At the site of the tear the various coats of the bowel had been separated and stripped asunder the prospects of satisfactory end-to-end junction seemed doubtful. Accordingly the duodenum was completely divided, the two ends were closed and posterior isoperistaltic gastrojejunostomy was performed. The man made a good recovery.

Surgeon Commander Rex Williams performed a successful operation in the case of a laceration of duodenum

W. B. Bracey aged 24, seaman as admitted from sea with penetrating wound of the right flank which resulted from a enemy bombing attack.

TABLE I.—RECOVERY RATE OF
INTESTINAL INJURIES

I Series of the small intestine	
Total number undergoing operation for injuries including small intestine	733
Number of recoveries	473
Percentage of recoveries	64
Number of operations for abdominal injury confined to small intestine	19
Number of recoveries	15
Percentage of recoveries	79
II Series of the large intestine	
Total number undergoing operation for injuries confined to large intestine	63
Number of recoveries	63
Percentage of recoveries	100
Representative 45% of all operations for abdominal injuries	
Sir Cathbert Wallace reported 30% in 1918	
[Sir Cathbert Wallace reported 37.5% in 1919]	
[Represent 27% of all operations for abdominal injuries]	
[Sir Cathbert Wallace reported 45% in 1920]	

Severe shock was present and as promptly treated. After an interval of approximately 12 hours after the receipt of injury the abdomen as opened through a right upper paramedian incision. The second portion of the duodenum was found to be almost completely torn across, and there were also penetrating wounds of the proximal jejunum and transverse colon. The duodenum was sutured in its transverse axis and the other injuries repaired in similar fashion. A foreign body was found 10,000

units of Bacillus Welch serum were introduced into the peritoneal cavity and the abdomen closed with a drainage tube. Recovery as uneventful. When he was seen 3 months later he had returned to duty and barium meal investigation revealed no abnormality in the stomach, which was empty in 4½ hours. The duodenal cap filled well, appeared normal, and was not tender. A large metal fragment was seen in the abdomen lying posteriorly behind the pyloric portion of the stomach.

Yet another case of a wound of the duodenum successfully treated is that of Mr. T. J. Cobbe

The patient, C. M. M., a mate, recovered from injuries due to fragment of bomb which not only damaged both walls of the stomach, but also wounded the duodenum and the colon.

Injuries of gall bladder and extrahepatic biliary tract. In this series there seems to be only one case of injury to the gall bladder. This was successfully dealt with by Miss E. M. Hall, F.R.C.S. There were multiple injuries including a penetrating wound of the abdomen, a perforated gall bladder and a ruptured liver were found at operation. The liver was sutured and the gall bladder was drained. There were

many other injuries affecting the skull, eyes, forearm, hand, etc., nevertheless, the patient recovered

Injury to biliary tract due to "blast" Kathleen T., aged 3 years, was the only survivor in a few houses which were completely destroyed by high explosives. She was the only living being when rescue parties arrived at the scene of the "incident." On admission to hospital she was in a state of severe shock. Apart from slight bruising of the right shoulder, there were no lacerations or external injuries. The abdomen was rigid and tender. After several hours the respirations became more rapid, and vomiting occurred. Operation was beyond consideration, a diagnosis of a ruptured diaphragm was tentatively put forward by me. After about 5 days the general condition slowly improved, the function of her bowel was restored, vomiting much less frequent. In 3 weeks' time the abdomen was becoming more and more distended in this lower portion, and its increasing size embarrassing both eating and movement. Twenty-five days after the "incident" the abdomen was opened under gas and oxygen, a large cystic swelling filling the whole abdomen was found, whose upper limit was not determined. Eight pints of bile-colored fluid were evacuated, and reported upon as consisting of "bile remnants." From this time her recovery was almost uneventful, and she is now well (Mr J. H. Buttery's case).

Injuries of the spleen The spleen has proved very vulnerable in this war, and has been damaged by penetrating injury, by subparietal crushes and by the effects of "blast." In such fatal nonpenetrating injuries from crushing mechanisms, burial, etc., as have come to autopsy, the spleen has been the organ most frequently damaged, when death has been solely or chiefly attributable to the abdominal lesion.

The recovery rate has been 55 per cent, which is a 10 per cent improvement on the figures of 1918.

Injuries of the appendix vermiformis In only 2 cases in this series collected from this war has there been any note of an injury to the appendix. In 1 case, the injury was inflicted by a revolver bullet, in addition, there were 4 wounds of the terminal ileum. The man recovered.

Injuries of the rectum In this present series, 52 per cent of patients with injuries of rectum have lived, an improvement on the 33 per cent recovery rate in the last great war (Sir Cuthbert Wallace). When the bladder is injured as well, 33 per cent recover.

Several cases have been observed of the explosive wound of the perineum, this seems to occur when the missile passes superficially across it. The sphincter surrounded by a circumanal ring of skin may be torn away from the surrounding skin, and may be drawn high up into the perineal tear. Mr W. B. Gabriel and Lieut. Col. Cameron MacLeod, R. A. M. C. have observed such a case in this war.

The value of the local employment of sulfanilamide powder in rectal injuries seems to have been clearly demonstrated in the successful case of a patient operated upon by Surgeon Commander Frank Stabler, R. N. V. R.

A Nazi officer in an E-boat was admitted to hospital with wounds in the back and buttocks from fragments of a shell from one of H. M. Destroyers. One of these splinters traversed the sacrum and damaged the underlying rectum. This posterior wound was excised, damaged fragments of sacrum were removed, and powdered sulfanilamide was insufflated in the track. Laparotomy was then performed, and a perforation of the rectosigmoid junction was sutured. A retroperitoneal hematoma was evacuated. No colostomy was performed. This type of case with bone injury, presacral blood extravasation and an associated large bowel injury did extremely badly in the last great war, the use of the sulfonamides marks a definite advance in the treatment of this type of case.

Injuries of bladder Penetrating wounds of the bladder have shown a recovery rate of only 35 per cent, which is rather lower than the 40 per cent of the last war (Sir Cuthbert Wallace). The recovery rate is approximately the same when the bladder is injured along with the rectum or colon.

The reminder to examine the interior of the bladder digitally, when there is perforation of that viscus, will often lead to the discovery of the missile. A bullet was even found lodged in the prostatic urethra (Major A. S. Till, R. A. M. C.).

Complicated abdominal injuries Multiple wounds of the abdominal viscera, especially the hollow viscera, manifestly render the prognosis of injuries to the belly more grave. The factor of serious concomitant hemorrhage makes the outlook still more serious.

A man was hit by a machine gun bullet. There was a small wound of entrance in left epigastrium over the left rectus at the level of the uppermost linea transversa, blood and air were bubbling out of this wound. Small wound of exit through left erector spinae, the level of which was about 1 inch lower than the en-

transverse wound. This wound was very small, bled very little, and was situated just lateral to the transverse processes. Lesions found at laparotomy included (1) perforating wound of anterior surface of stomach, close to greater curvature with severe bleeding from this perforation, about $\frac{1}{2}$ inch in diameter; (2) posterior surface of stomach wound of exit into lesser sac with very little extravasation; (3) perforation anterior surface of terminal part of duodenum close to duodenojejunal junction there was severe bleeding from this wound; (4) perforation of posterior surface of duodenum, but comparatively little extravasation; (5) severe bleeding from transverse mesocolon (right colic vessels); (6) large bowel in condition of spasm, small bowel dilated and immobile. The case ended fatally.

Two wounded patients were admitted simultaneously to the same hospital, an old woman of 78 years and a girl of 3 years. Age perhaps did not play such an important part in determining the final ending, for in each case the injuries were of multiple or severe character. In the case of the old lady (Mr. H. R. S. Harley's case) there were present (1) laceration of upper and outer part of the right thigh involving the deep fascia; (2) compound fracture of the trochanteric region of the left femur with retained foreign body; (3) 6 lacerations of the buttock; (4) Pott's fracture of the left ankle; (5) laceration of scalp; (6) tender rigid abdomen in which autopsy revealed much blood, and large perforations of the jejunum. A retained fragment $\frac{1}{4}$ by $\frac{3}{8}$ inch was present.

The child of 3 years was admitted a quarter of hour after the incident in condition of extreme shock. A single wound covered with brick dust was present, and from it there protruded several feet of dust covered small intestine. After intensive resuscitation, the small intestine was washed and replaced inside the abdomen by Mr. Wain in incredibly brief space of time. Despite every measure death ensued.

An officer at the termination of a parachute descent, landed in the fork of a tree, and received penetrating wound of the rectum, a branch disrupting the pararectal tissues right up into the iliac fossa, the peritoneum was torn. The injured man then fell to the ground sustaining severe fracture of the pelvic girdle. There was a wide separation of the symphysis and disruption of the sacrospinous symphysis. He survived his injuries about year.

On the other hand some cases have made splendid recoveries.

R. H. R. male was injured by a splinter of bomb and sustained damage to stomach, transverse colon, and small intestine. There were also injuries to the right kidney, left leg, and left arm. The wounds of the stomach and small bowel were sutured. The colon was so severely damaged that a resection of a piece of the large bowel was necessary. Recovery (Case of Mrs. G. M. B. Toland F.R.C.S.)

C. W., male, aged 34 years, as admitted to hospital half hour after the incident. He is found to be suffering from the following injuries: (1) penetrating wound over the middle of the upper part of the right rectus abdominis. Examination of the abdomen demonstrated rigidity and generalized tenderness; (2) through-and-through wound of the middle of the left thigh with retained foreign body, but no bone injury; (3) penetrating wound of the left leg with a retained foreign body; (4) superficial laceration of the buttock. Operation took place 6½ hours after injury. Surgeons (Mr. Wain and Mr. Thomas) co-operated. Three pints of blood were found in the peritoneal cavity. There was a wound of the greater curvature of the stomach, near the pylorus, a wound of the transverse colon and 7 wounds of the small bowel, from one of which a bomb fragment was removed. All these perforations were sutured. A rent on the inferior border of the liver which was not bleeding, was left alone. Recovery took place.

A sailor with almost every region of his body damaged, including his small intestine was successfully operated upon by Surgeon-Commander Frank Stabler R.N.V.R.

The man was hit by cannon shell 6 hours before admission to a naval hospital. He had the following injuries: (1) frontal region laceration with fracture of outer table of skull; (2) punctured wounds of abdomen above pubis, which had produced 6 perforations of jejunum about feet from duodenojejunal flexure; (3) right hand, index and middle fingers blown off with metacarpal compound fracture and two penetrating wounds; (4) compound fracture of left olecranon; (5) 9 punctured wounds of left thigh; (6) punctured wound right thigh; (7) compound fracture of left patella. Seven inches of bowel were exposed including 5 perforations; the sixth perforation was treated by separate suture. No drainage was employed in the space of hours. pints of blood and plasma were given.

It is associated severe fracture especially a compound fracture loads the scales heavily against the victim with an abdominal injury; a smashed femur complicating a belly wound or contusion especially at its upper extremity is a burden hardly to be borne by suffering humanity.

Nevertheless, such patients have survived.

Mr. Kenneth Bond had under his care a bomb injury admitted with small opening close to the anus which led into large cavity on the right side of the rectum and involved complete division of all the sphincters including the anorectal ring. The man had also sustained multiple fractures of the anterior portion of the pelvic ring, and an incomplete rupture of the urethra. Finally double spiral

fracture of the right femur completed the list of his injuries. The end-result consisted in a complete recovery of function of all the systems involved.

A patient of Mr F G Wrigley actually survived an *injury to the abdomen and a compound fracture of both femora*.

This patient (Mr F G Wrigley's case) received a bomb injury to abdomen, with contusion of colon, damage to omentum, extensive extraperitoneal wound of lower left iliac region, bilateral compound fracture of femur, wounds of right forearm, and right temporal region. She recovered from the abdominal injury, although a fecal fistula formed 4 months later. She ultimately succumbed from mental deterioration and the effects of sepsis in connection with one of the wounds of the thigh.

In a patient who was under the care of Mr A L Candler, after she had received a *penetrating wound of the abdomen and a fracture of the right femur*, a completely successful result was obtained.

This occurred in a woman of 30 who was putting out incendiaries on the night of an intense raid on a city. On admission to hospital, shock was extreme. After measures for resuscitation had been employed, laparotomy was performed, and several intestinal perforations sutured. The hospital was badly damaged the night following, and the woman was transferred to an infirmary in another town, her pulse was 120 after her transportation. Her subsequent course was punctuated by several alarming or disquieting incidents, large quantities of pus and blood were passed by the rectum, and a transfusion of 3 pints of blood on one occasion was required. A few days after this a small intestine fistula appeared at the bottom of an unhealthy-looking abdominal wound. This finally healed, the patient making a complete recovery.

An unusual mode of wounding was noted in the case of R A C who was blown by the blast wave from a detonating bomb on to the roof of the car beside which he was standing. Then came a second bomb, from which he received 16 superficial splinter wounds of the left lower limb, but also a penetrating injury of the belly. No visceral injury was discovered on laparotomy. The man recovered.

It is possible for those persons who are *maimed by high explosive*, in addition, to *suffer from burns*.

H W W, male, aged 46 years, was extinguishing an incendiary bomb with sand when it exploded. He received burns of the face and hands, and 4 punctured wounds of the abdomen. At operation, 1 large and 1 small wound of the ileum were sutured, as well as a small tear of the transverse colon. He recovered.

ABDOMINOTHORACIC INJURIES

Uninformed lay opinion is prone to associate penetrating injuries of the trunk with a dire mortality, and statistical inquiry only too truly confirms the fatality of wounds involving certain lethal anatomical areas, and the severity or serious consequence of many wounds of the less mortal regions of the thoracico-abdominal zone under conditions of modern warfare. The behavior of wounds of the diaphragm itself had been known to surgeons since the days of Ambroise Paré, and was accurately noted and discussed by Guthrie when writing of the war surgery of the Napoleonic era. The operative treatment of thoracic wounds by Guthrie and by Baron Larrey, Napoleon's great Surgeon General, anticipated, though in immature fashion, the modern treatment of wounds of the chest received under conditions of war. The early story of the abdominal aspect of the problem has already been told.

Injuries which involve thorax, diaphragm, and abdomen may be of penetrating or of non-penetrating character. In the war of 1914-1918, the first named group completely overshadowed and outnumbered those which were subparietal lesions, in this present conflict the cases for which surgery is possible still belong almost exclusively to the former class.

Penetrating injuries. In one series of cases from the war of 1914-1918 (Sir Cuthbert Wallace, 1922) abdominothoracic cases constituted 12 per cent of the abdominal cases which reached the casualty hospitals of one army, the operations performed on this group of patients also accounted for 12 per cent of all the abdominal operations in that army. In the Spanish Civil War the percentage of the bellies admitted to a hospital of first urgency was not dissimilar to that which obtained in 1914-1918, i.e., 11 per cent (Jolly, 1940). Abdominothoracic injuries in the present series of abdominal injuries from this war approximate 13 per cent, the ratio is therefore not dissimilar to those of previous campaigns.

Statistics of abdominothoracic wounds culled from the official history of the war of 1914-1918 demonstrate that in a vast majority the abdominal lesion determines the gravity of the prognosis, and, further, that wounding of the

hollow abdominal viscera greatly augments the fatality of the injury. It will at once be apparent that the anxieties occasioned by a wound of the left dome of the diaphragm must greatly exceed those which are aroused by right-sided penetration of the midriff. An analysis of cases from this war confirms the truth of both these statements.

Of 78 abdominothoracic injuries in this present series 42 were right-sided and 36 were left-sided. Forty nine patients survived, i.e., a recovery rate of 63 per cent, a figure which very nearly equals that attained by 6 surgeons of the Fourth Army in 1918 during the last great war. In this present series 70 per cent of the patients with right-sided abdominothoracic wounds lived whereas only 50 per cent of the left-sided abdominothoracic patients survived.

An excellent classification of penetrating abdominothoracic wounds has been given by my friend Tudor Edwards

- 1 The chest and abdomen may be penetrated by separate missiles, the wounded man sometimes becoming a veritable St. Sebastian, his abdomen and chest riddled with fragments of high explosive or machine gun bullets.

- 2 Missiles may penetrate the chest and may emerge through the abdominal wall or be retained within the belly. On the other hand, the track of the missile may be in the reverse direction—the wound of entry in the abdomen and the fragment retained within the thorax.

- 3 Traversing wounds of the lower chest, especially if inflicted during expiration may pass through the diaphragm and occasion damage to the abdominal organs lying immediately subjacent to the midriff.

- 4 Tangential wounds of the lower thorax in which considerable damage, including diaphragmatic injury and perforation is produced by the missile and in-driven fractured ribs.

The diaphragmatic lesion. The present war series confirms many of the findings of a quarter of a century ago. The injuries of the diaphragm in abdominothoracic lesions are still mostly found in the sloping muscular portion and are especially frequent when this lies in contact with the thoracic wall. In cases that come to operation the rent is usually small. In one series the linear tear was half an inch long

or less in 50 per cent of the cases. Many openings are mere punctures. Larger irregular apertures in those suitable for surgery are seldom found to be more than $1\frac{1}{2}$ to 2 inches in diameter.

Lockwood and Nixon (1918) compared the cardiac and respiratory embarrassment due to a rent in the diaphragm to that produced by an open pneumothorax. On the other hand for Sauerbruch the importance of the diaphragm in relation to respiration and the circulation was exaggerated. The great improvement in the recovery rate of abdominothoracic cases after the diaphragm began to be sutured by British surgeons in the last war may have been partly due to the repair of that muscle but also to the improved treatment of the thoracic condition and increasing familiarity with the many problems of war surgery. Small wounds undoubtedly heal spontaneously and others are at least temporarily plugged by omentum, spleen, liver stomach, etc.

Wounds of the central tendinous part are obviously more serious than those at the periphery but some have survived. A century ago Guthrie published notes of a man with a wound of pericardium left ventricle lung liver and the tendon of the diaphragm. The man survived for 4 or 5 months. He suffered from palpitation and uneasy sensations in the chest, and died of bronchitis. Fuchs (Sauerbruch and O'Shaughnessy 1937) successfully operated upon a patient with a stab wound of the right ventricle which also perforated the central portion of the diaphragm. The track passed obliquely inwards from the fifth sternochondral articulation and was thought before operation to implicate the stomach.

Diagnosis of penetrating abdominothoracic wounds. Doubt may sometimes be felt at first whether the gravity of the condition of a man with an abdominothoracic wound is due to the thoracic, to the abdominal or to other concomitant injury. Nixon (1919) who had great experience of these cases thought that if there is a fair air entry into the lungs thoracic injury is not to be held accountable.

The anatomical site of the aperture of entry and of exit in a traversing wound of the trunk limits the track of the missile with fair accuracy. The position of the patient at the time of

injury also demands consideration, the structures probably damaged may then be readily adumbrated. In cases in which a fragment of metal, spicules of broken rib, etc., are retained, radiological investigation is indispensable, its necessity in estimating diaphragmatic movements and thoracic pathology cannot be overestimated. There are also clinical signs and symptoms which arrest attention and which may clarify, or may, on the other hand, obscure, the diagnosis.

1 Abdominal rigidity does not of necessity betoken involvement of the subphrenic viscera. It is well known that injuries of the pleura or lung, especially if situated in proximity to the diaphragm, may occasion abdominal rigidity and may arouse suspicion of an abdominal lesion.

2 Sickness and vomiting have been known to occur in cases of lower thoracic injury, but are more frequent in abdominal lesions, as is eructation of gas.

Diaphragmatic injury is suggested by an almost entirely thoracic type of respiration, with a catch at the end of inspiration, sometimes a definite spasm or hiccup, yet the actual respiratory rate may be little altered. In the late stages of injury to the diaphragm there is fixed pain, exaggerated on exertion and referred to clavicle or scapula according to the position of the injury or location of the retained missile. Pain is induced especially by lifting, coughing, or even deep respiration. The diaphragm is kept motionless on the affected side.

The diagnosis of a wound of the diaphragm is not easy in subparietal injuries. The syndrome of tension pneumothorax may be simulated by the sudden irruption of stomach or colon into the chest. Radiology and the determination of the intrapleural pressure enable a correct diagnosis to be attained.

The existence of *blast contusion of the lung* is now well established on clinical and x-ray evidence and by postmortem findings, and the dangers attending the use of inhalation anaesthesia in these cases are overwhelming, great caution must therefore be employed when this is suspected, yet blast contusion of the lung is sometimes only the index of perhaps graver changes in the organs below the diaphragm.

Other serious cases may have been in very close proximity to detonating bombs, and may be suffering from a dangerous and grave degree of saturation of the blood by explosive gases, such as carbon monoxide or nitric oxide. The severity of the clinical state may even be due to such lesions as myocardial trauma. Such possibilities should not be overlooked amid the circumstances of this "total" war, their presence and the existence of other grave multiple injuries heavily load the scales against recovery.

Penetrating injuries by large missiles. The injuries produced inside the chest or abdomen by large fragments of metal or other foreign body are almost always irrecoverable, the result is scarcely likely to be different in those wounds if more than one cavity of the body is implicated. There was in the Royal College of Surgeons' Museum till the time of its destruction a piece of brass tubing, $4\frac{3}{8}$ inches long, removed by Mr. Reginald Vick in Macedonia from a Greek soldier, who recovered after the simple extraction of the missile, which had passed from the middle of the right scapula and projected in the epigastrium (Gordon-Taylor, 1939).

Saint (quoted by Gordon-Taylor) had a successful right-sided abdominothoracic case in which a fragment of shell weighing 2 ounces had traversed chest, diaphragm, and liver and produced 2 perforations of the duodenum and 1 in the hepatic flexure of the colon.

In one of my patients, the successful result of whose case is recorded elsewhere, a missile weighing nearly 4 ounces produced the most grievous damage inside the belly and fractured the bony wall of the thorax (Gordon-Taylor, 1919), the diaphragm was apparently uninjured. In the penetrating abdominothoracic wounds which form a section of the series collected from this war, there is no record of any case that controverts the reputed fatality of the large missile when it wounds the trunk.

Treatment of penetrating abdominothoracic injuries. This contribution is largely concerned with the surgical treatment of injuries of the diaphragm and of those abdominal organs whose anatomical proximity renders them specially vulnerable in cases of diaphragmatic wounding.

Treatment of wounds implicating the liver
The dimensions and the velocity of the missile play an important part in determining the type of hepatic lesion, which may be almost protean in character. Large fragments of liver may be torn off, and as much as one third of the right lobe has been found loose in the peritoneal cavity of a patient who recovered from a right-sided penetrating abdomino-thoracic injury in the last war.

Before their total destruction the specimens in the Royal College of Surgeons War collection illustrating gunshot wounds of the liver revealed many lesions for which any surgery must be futile or incomplete: thus it would be impossible by operative measures alone to prevent infection throughout the length of a ragged track running from the right lateral surface of the organ to its extreme pole on the other side of the body. In many cases of liver injury due to enemy action there are few arresting clinical signs and it is significant that out of all the penetrating injuries of the abdomen which recovered in the last war without operation the wounds were mostly situated in the liver area. Surgical intervention directed towards the liver is indicated under the following circumstances only: (1) gross hemorrhage from the liver which mainly depends on whether large veins in the organ have been injured—hemorrhage otherwise ceases spontaneously as does oozing of bile unless main ducts are severed; (2) the association of some thoracic or another abdominal lesion demanding exploration; (3) the retention of a missile in the liver especially a large missile in an accessible position in that organ. In the case of severe laceration of the liver packing may be necessary to control hemorrhage. In some such patients the diaphragm may be sutured, and the thorax closed in the approved manner with airtight drainage of the pleura by means of a Malecot tube inserted through a separate intercostal incision. The gauze pack is brought out through another separate incision in the anterior abdominal wall. In other cases the diaphragmatic opening may be enlarged parallel with fibers from mediastinal to lateral border the diaphragmatic edges are now approximated to the intercostal muscles and the pleura is thus shut off from the drainage track.

Early jaundice in cases of hepatic injury may be present, and is usually slight and evanescent; the possibility of a collection of bile in peritoneum or pelvis should always be considered. Late jaundice has a much graver significance, and indicates serious infection.

Secondary hepatic hemorrhage in penetrating abdomino-thoracic injuries is almost always fatal, and is usually associated with signs of sepsis such as pain, elevation of temperature and pulse rate, abdominal pallor, restlessness and loss of strength.

The formation of an intrahepatic abscess round a retained fragment may be dealt with successfully by surgical measures.

Treatment of gunshot injury of the spleen. A study of the specimens of gunshot injury of the spleen in the war collection formerly housed in the Royal College of Surgeons used to suggest that wounds of that organ are frequently complicated by damage to adjacent viscera; yet in some collected clinical series it is stated that in more than half the cases of splenic injury revealed at operation there was no damage to other abdominal organs. This was certainly not my experience (Gordon Taylor 1939) which is in agreement with that of Major Jolly in his surgical work with the Spanish Republican Army (Jolly 1940).

The propriety of primary splenectomy in cases of gunshot injury still remains a subject of controversy. The removal of the organ should certainly not be resorted to lightly heartedly but in my opinion the procedure has not greatly increased the risk. The suture of the spleen may not be difficult when the organ is approached through the chest and diaphragm, but when explored by other routes cobbling of the organ is wasteful of time and may leave a sense of insecurity. Jolly (1940) and some of the Spanish surgeons write enthusiastically of splenectomy.

Numerous cases of successful transdiaphragmatic splenectomy in left-sided abdomino-thoracic wounds were recorded in the war of 1914-1918, some of which were associated with the operative repair of injuries to the stomach (Richard Charles, George Gask, J. E. H. Roberts, A. L. Lockwood, Gordon Bryan, Gordon-Taylor etc. and very recently by Valentine Logue). In the last war recovery has even

taken place in cases of left-sided abdominothoracic wounds in which left-sided nephrectomy as well as splenectomy had to be performed for complete disruption of each organ (Gordon-Taylor) and also in the present conflict (J Scholefield)

Treatment of wounds of the pancreas These injuries were less frequent in the war of 1914-1918, or at any rate were less often recognized, than injuries of any other of the abdominal viscera, it is not otherwise today. The intimate anatomical relation of the gland to the large blood vessels doubtless explains the paucity of wounds coming under the observation of the casualty hospital surgeons, doubtless some are unrecognized and are designated retroperitoneal hematomas. I have knowledge of only 3 abdominothoracic injuries implicating the pancreas in which recovery took place in the last war (Saint, Alan Curry, Gordon-Bryan), there are none in the present series from this conflict.

Treatment of injury to the kidney Each kidney is equally liable to damage. It was estimated that in 40 per cent of gunshot wounds of the kidney investigated at an English surgical base in France during 1914-1918 the thorax was also implicated. The propriety of immediate operation on the kidney in abdominothoracic wounds demands even more careful consideration than in purely abdominal injuries. Probably the best course is to excise the wound leading down to the damaged kidney, the organ can then be inspected and any foreign body removed.

In the majority of cases the renal injury plays a minor part in menacing life, and only for severe hemorrhage, a hopelessly pulped organ, or gross damage to the renal pedicle is primary nephrectomy indicated. In about 20 per cent of cases of gunshot injury of the kidney in the last war, life was threatened by secondary hemorrhage, consequent on sepsis, a retained missile, or an infarct of the kidney produced by damage to some branch of the renal artery, secondary hemorrhage is an infrequent phenomenon today.

Treatment of injury to the hollow organs Of hollow organs the stomach and splenic flexure of the colon are those most liable to injury, in suitable cases transdiaphragmatic laparotomy

affords excellent access to these organs. Concomitant involvement of the small intestine denotes a more vertical track of the missile, and demands a separate approach or a much extended incision, such a measure, though necessary, increases risk to life. Multivisceral damage also augments mortality, and vertical wounds, which may even extend from supraclavicular fossa to femur, tend to be very fatal.

The possibility of injury to the duodenum must always be borne in mind, and any hematoma in its vicinity should be suspect, lest a retroperitoneal rupture of this fixed part of the small gut be overlooked. Every abdominothoracic case in the present series associated with a laceration of the hepatic flexure has perished.

Summary of treatment The treatment of penetrating abdominothoracic injuries may be summarized as follows

- 1 In many traversing (through-and-through) abdominothoracic wounds of the right side produced by a small bomb fragment or bullet *no immediate active surgical treatment* is required, provided that (a) no gross damage has been inflicted upon the thoracic or abdominal wall—fractured ribs, explosive effect, etc., (b) the direction of the track of the missile does not appear to compromise the general peritoneal cavity or suggest the desirability of its exploration, (c) the signs of abdominal hemorrhage or of injury to a hollow viscus are clearly absent.

- 2 In cases of right-sided abdominothoracic wounds in which a small fragment is retained in an inaccessible position in the substance of the liver an *expectant line of treatment* is the correct procedure, accessible fragments, unless small, should be sought and removed.

- 3 When there is an open, blowing thoracic wound or an associated "stove-in chest," the chest injury must of course assume chronological priority of treatment.

- 4 If the position of the wound of entry and exit in a left-sided abdominothoracic wound adumbrates a track implicating that fatal left subphrenic area of the abdomen, or if a radiograph demonstrates a fragment of metal retained in this region, the thorax should be dealt with first and access to the upper abdomen obtained through the diaphragm.



Fig. Entrance Hall of the Royal College of Surgeons of England showing the destruction effected by the bombing on the night of May 9-10 1941.



Fig. Room 5 in the Museum of the Royal College of Surgeons showing the destruction of the room and its galleries. The bust of John Hunter is enclosed in a rampart of bricks.



Fig 3 Room 5 which contained the majority of the comparative anatomy specimens belonging to the Museum which started with the original Hunterian collection



Fig 4 This shows amid the debris of Room 4 the bust of the naturalist, Owen, a former conservator, which was only partially damaged

5. When the thoracic injury appears insignificant, but there is evidence of severe widespread intraperitoneal damage especially in involvement of hollow viscera, the abdomen should be explored through an appropriately placed laparotomy incision. This instruction applies to wounds of thorax and abdomen produced by the same or by separate missiles.

6. When the thoracic injury seems slight, and when the evidence of a radiograph or the direction of a missile track in a through-and-through wound suggests an extraperitoneal course of a small fragment such an abdomino-thoracic injury may often be left alone.

If in such cases there is evidence of injury to the kidney the parietal wound down to the kidney should be excised the organ investigated, and any foreign body removed.

7. In cases in which the thoracic wound is situated low down on the lateral or antero-lateral aspect of the chest access to both supra-diaphragmatic and infradiaphragmatic areas may be obtained by cutting through the costal arch after the manner of Bland Sutton, Duval, Bérard, etc. this method of access is undoubtedly severe.

8. If an abdominothoracic injury has been approached from the abdominal aspect it is important not to waste time trying to complete a difficult suture of the diaphragm in a critically ill patient, unless the aperture in the midriff is so large that immediate or early herniation of the abdominal contents is certain to occur.

Nonpenetrating abdominothoracic injuries. There are no successful operations for sub-parietal abdominothoracic injuries indisputably involving the diaphragm in this present series of cases. The inference is that these cases involve such desperate or multiple injuries that death ensues. Some such cases are found at autopsy. The experience of this war so far goes to show that abdominothoracic injuries due to fragments of high explosive or bullets are far less grave than those due to crushing force or the effect of blast.

A man of 5 years was admitted to hospital after having been dug out from under the debris of a house. He showed no marks of external injury, complained of no pain, distress, and as only slight dyspnea. On the following morning he was dyspnoeic

and complained of pain in the left chest. These symptoms increased during the day. On examination he was tympanic over the left chest up to the third rib. Percussion and his heart as displaced to the right. A ray suggested diagnosis of collapse of the left lung, pneumothorax, and a pleural effusion. Just above the fluid level were some vague shadows which were thought possibly to indicate the presence of the thorax of gut. However on the supposition that the condition was tension pneumothorax, a needle was inserted in fourth intercostal space anteriorly and about liter of air was let out with great relief to the patient. The process was repeated, and the needle was connected with receiver by means of rubber drainage. Fluids taken by the mouth escaped through the needle in the thorax. The patient was finally operated upon and ten in the diaphragm found, through which an enormous hernia of the stomach had taken place. Death occurred.

Mention has already been made of the advancement of the science and craft of surgery through the stimulus of war. The familiarity with the transdiaphragmatic approach to the vault of the abdominal cavity attained in the latter years of the war of 1914-1918 has been turned to useful purpose by thoracic surgeons since the war. The advances in this field are stupendous. Diaphragmatic hernia, especially that produced by injury is nowadays approached by the thoracic route in Britain. The operation of cardio-omentalopexy gave good results in the late Mr. O'Shaughnessy's capable hands, and improvements in the technique of the operation have been effected by Mr. John B. Hunter. The general surgeon also avails himself of a thoracic approach in the operation for the surgical removal of the lower end of the esophagus or of the cardiac end of the stomach.

Increasing familiarity with thoracic surgery doubtless provided the stimulus for Pierre Duval's successful operation for the extraction of a bullet from the suprahepatic portion of the inferior vena cava. The sternum was split, and the diaphragm divided backwards to the caval opening in the midriff. To my mind this still remains the most brilliant operation in the history of surgery.

CONCLUSIONS

1. Despite the gravity of the wounds and the frequent association of multiple injuries, approximately 50 per cent of the patients with

abdominal injury for whom operation is possible survive

2 The military situation permits of no information as to the percentage of all abdominal casualties for which operation is possible

3 The percentage of recoveries for injuries to the stomach, the small intestine, and the spleen is actually higher than in 1914-1918, though the recovery rate for the large bowel is the same

4 Few patients have survived after lengthy resections of bowel

5 The employment of the sulfonamide locally and by oral administration has proved of inestimable value

6 The transfusion of blood or the blood derivatives has been employed on a liberal scale and this method of treatment has made a host of patients operable who would otherwise certainly have died

THE CARE OF THE LIGHTLY WOUNDED

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THE main thesis of my remarks is that far too little attention was paid in the last war to the care of the lightly wounded. By lightly wounded I mean wounds which do not involve any of the body cavities, such as the head, chest, or abdomen or any bone, major blood vessel or nerve. Most of these patients were ambulatory and, had they received prompt surgical attention, should have been able to return to duty within a few weeks. As a group they represented a considerable majority of all the wounded.

We were told that the main duty of the Medical Corps was to maintain the strength of the fighting forces yet the primary attention as well as the large majority of the time and effort of the surgeons was directed to the care of the severely wounded, very few of whom ever went back to duty. The lightly wounded "waited for the second table and got the leftovers." This was quite in keeping with our peace time training and humanitarian desires. If our main object is to save life those dangerously wounded should come first but if our main object is to win the war and maintain the fighting forces it would seem that the men who might go back to duty should receive at least equal attention and that the attempt should be made to reduce their period of disability to the minimum.

As I am expressing a purely personal and individual opinion I may be allowed to recount the experiences on which that opinion is based limited though they were. Going over with the Presbyterian Hospital Unit in May 1917 we were assigned to the British Expeditionary Force and No. 1 General Hospital at Etretat near Havre was turned over to our care. At the time of our arrival in France things had been relatively quiet for some time and most of the patients then in the hospital had been

sent down from the front area several weeks before. The main problem seemed to be to get the severely wounded patients well enough to be sent across the channel to England. These included patients with badly infected compound fractures, chest wounds, and a few who survived after abdominal injury. Also there was a large number of ambulatory patients with small infected wounds, many of whom had been under treatment for weeks and even months. In addition to their local wounds they had become soft and flabby and their morale very low. When their wounds finally healed they were sent to convalescent camps for more weeks of rehabilitation before going back to the rest areas to rejoin their divisions. When a train load of 300 to 700 new patients arrived at the base all hands concentrated on the severely wounded and those patients with minor injuries waited until all the others had been cured for. As the wounds by that time were 3 to 10 days old, not much was done except daily dressings by the junior medical officers or more usually the nurses.

After the Somme the British Expeditionary Force realized that the wounded could be handled better if their operative treatment was carried out nearer the front lines. In preparation for the battle of Passchendaele in July 1917 operating teams were sent from the base hospitals to the casualty clearing stations which were stationed 5 to 10 miles behind the lines and usually at a railroad. The patients came from the field hospitals to the casualty clearing station by ambulance and from there were sent down by train. They usually reached the hospitals 4 to 12 hours after injury. These hospitals were entirely housed in tents except for a Nissen hut for the operating theater. When we arrived on July 23 1917 there were 3 groups of these hospitals back of Ypres with 3 or 4 hospitals in each group. We were assigned to No. 47 Casualty Clearing Station with 7 other surgical teams. Each team consisted of a surgeon, an anesthetist, a nurse and an orderly. The duties of the

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operating team were twofold, to serve in the admitting ward and in the operating theater. In the former, wounds were merely inspected, dressings changed, and the decision made as to whether the patient should go to the resuscitation ward, preoperative ward, or be held for evacuation on the next train. When a rush was on, the admitting and sorting was done by one of the other medical officers. The operating teams were on duty 16 hours out of the 24 so there were 6 teams operating from 8 a m to midnight, and 4 from midnight to 8 a m. The plan in our group was for the ambulances to bring all patients to one hospital until 200 had been admitted, the stream then being diverted to the second hospital. By the time the third had admitted its quota, the first hospital was supposed to have finished with its group and be ready for the next. During a push, of course, the numbers were far greater than in the intervening times. During a lull it might take 24 hours to get our quota of 200 but on the second day of the first push we rotated 6 times, each hospital getting over 1200 patients. The worst cases, except for those patients obviously moribund, were operated on first. One severe case an hour was about the average that one team could handle. This meant that during the busiest period only 10 per cent of the patients received could be handled in the operating theater. The rest had to be sent on to get their operative care later on, perhaps the next day, perhaps a week later. This failure to give the lightly wounded early operative treatment was a necessity during rush times but the peak load necessity seemed to establish the general policy at all times, and general policies in the British Expeditionary Force or any army are hard to change. This I discovered during one quiet period when only 2 teams were on call. I took my team to the receiving tent and under gas operated on some of the patients with minor wounds who, as I had seen at the base hospital, required months to get back to duty. If operated upon early I thought they might recover within a few weeks. We were able to care for quite a few cases in a short time. Soon word came from the Commanding Officer "Sorry, but that's not done in the B E F." This same general plan seemed to hold in

other casualty clearing stations in our area. The French had already established the wisdom of early surgical treatment of minor wounds and during quiet times were doing a good deal of it in their advance hospitals. Coming back to the base hospital, I was again impressed with the long delay in healing of those minor wounds whose only early treatment was dressings, or occasionally some bipp paste.

After 14 months with the British I was transferred to the American Expeditionary Forces in the latter days of the battle of Château-Thierry. During this and the St Mihiel drive the problem was to meet the actual necessities with the materials at hand, but later in the Argonne, with more hospitals and better organization, the problem of providing the wounded with early surgical treatment was well met. In addition to a goodly number of evacuation hospitals, well equipped and with surgeons of experience, several mobile hospitals, notably Nos 1, 2, and 4, were set up sufficiently far forward to give the severely wounded an excellent chance for recovery. Yet here again, in both evacuation and mobile hospitals the major emphasis was placed on giving the severely wounded the right of way. The others were either attended to after the severe cases were finished, or were immediately sent down the line. In a few places operating teams were assigned to the lightly wounded group. Sherbondy and George Davis by using 3 tables, orderlies, and nurses proved that they could handle 6 to 8 cases an hour. At the time of the Armistice, Colonel Grissinger of the First Corps had plans all ready for execution for a special hospital well forward for the lightly wounded patients only, but it was never opened.

That early operative treatment of minor wounds will shorten tremendously the period of disability was proved at the hospital for the Army of Occupation in Coblenz. In the first month we had 83 cases of gunshot wounds all due to careless handling of firearms. This led one old regular to say "I always claimed that a soldier was the last person in the world to be trusted with firearms."

I have a vivid memory of a dressing station along the road that ran north from Ypres

along the canal. Here in a small cellar an attempt was being made to revive a patient with a badly shattered thigh and a perforating belly while huddled up behind what was left of the front wall of the house was a group of walking wounded waiting for transportation. Again at the field ambulance tired men were working over a row of stretchers, while near by a large group of walkers squatted down or curled up on the ground waiting for transportation. Near by was the narrow gauge railroad with its cars of shells coming up, and the cars going back—empty. Lorries were going up the road full of supplies of one sort or another and others going back—empty, yet the walking wounded waited for ambulances. Again at the casualty clearing station when the ambulances arrived—patients on stretchers were cared for first while the walkers waited. Their dressings were changed, they were fed and berled to one side to await transportation by the next train to go down. I can see them when the train arrived at the base. Again the stretchers came first in the ambulances, while the walkers, who could slowly plodded the half mile from the railway station to the hospital. It sometimes took 24 to 48 hours of operative work to care for the severely wounded before the others could have their turn. It was too late then for any preventive work and for early healing. One found just dirty granulating wounds, often with insufficient drainage. Then came the long, slow weeks of healing with a gradual softening—physical mental and spiritual. This was the forgotten man.

In the Argonne the picture was similar. In the divisional triage as the stream of wounded men came in they were sorted out and passed down to the mobile and evacuation hospitals. Again the major attention and time were given to the severely wounded while the lightly wounded received either delayed treatment or were sent directly on with a mere change of dressing. These were the men however who if they could have had operative treatment early might have rejoined their units within a few weeks. Of the patients with severe injuries of the head chest belly or with compound fractures and tight calves very few even resumed active duty.

So much for the past. Can we profit by that experience in planning for the days that lie ahead? In times of retreat and especially the conditions the British faced in the days preceding Dunkirk little can be planned or carried out. The main problem is to get the wounded away at all. Any operative treatment must be delayed until they have been brought a long way to the rear. In stationary warfare or in times of an advance hospital facilities can be brought reasonably close, and operative treatment carried out early.

The surgical care of the lightly wounded varies from that of the more serious cases in several ways. Many of the latter patients need attention before they come to the operating table hence the need for resuscitation wards for combatting shock. Such a measure is unnecessary for the lightly wounded. In the operating room there are three periods first, the preparation of the patient and the induction of anesthesia second, the operation itself and third the application of dressings and splints when necessary. In cases of major wounds the operation will require 60 to 90 per cent of the total time. One operator can use 2 tables at the most the next patient being prepared as he operates and the last stage of operation being carried out by an assistant as the operator starts anew. With the minor wounds the time of operating may not be greater than that required for preparation and may be even less. One surgeon could handle 3 or possibly 4 tables with the appropriate number of assistants. While 1 serious case an hour can be used as a general figure for what one surgeon could handle with proper assistants he could operate on 6 to 8 minor cases.

After operation the serious cases will need a good deal of careful attention for hours and even days. The organization of postoperative wards and personnel is quite different from that needed for the later care of the minor wounds. Many of the patients with serious injuries are actually nontransportable for days and will do much better if they are not moved for a much longer period. Most of the patients with minor injuries could be transported within a few hours or a few days at most. Therefore is it not worth considering to arrange for entirely separate units to handle these 2

groups of cases? Each unit should be planned and organized according to the needs of the group assigned to it. As the stream of wounded starts back the two groups should be separated early. A large majority of the lightly wounded might be transported back in the supply trucks on their return journeys, the ambulances being used for the serious cases. Certain hospitals should be designated and planned only for the care of patients with minor injuries. Such hospitals should plan for a routine somewhat as follows. On arrival the patients would be examined by an experienced surgeon to pick out those sent by mistake who belong in the more serious group, and mechanism provided for their immediate transfer. The suitable cases then would go to the x-ray department for localization of foreign bodies. After this they would go to the preoperative ward for removal of clothing and rest until the operating theater was ready for them. In the operating room each surgeon would have 3 tables at his disposal and 3 teams. The patient would be placed on the first table, the first team preparing the field and giving the anesthetic. The same team would repeat this performance on the second and third tables. The surgeon and his assistant would follow after and débride the wound, treating by primary suture or packing with or without the use of chemotherapy and dictating orders for later care. The third team would then take over, apply the dressing, bandages, and any necessary splint. The patient would then be taken to the postoperative ward. If the lighter forms of anesthesia were to be used, either inhalation or intravenous, immediate after-care of these patients would be much simpler

than that of the more serious cases and would require a smaller personnel in these wards. With the exception of some of the lower extremity cases most of these patients would become ambulatory in a short period of time. This would simplify the feeding problem. At the time of operation the surgeon should be able to make a fair guess as to whether the patient should be retained or early returned to his unit or sent farther back for prolonged treatment. Final decision, of course, would have to be checked before discharge. This plan seems reasonable to me. In this way this "forgotten man" might be remembered and his minor wound prove to be a minor affair and not a cause of months of disability.

Many of us believe that the only kind of war casualties we will have to face in the near future, outside of the Navy, will be those resulting from bombs. Looking after the wounded civilian population may not be maintaining the fighting forces in the field and it may not be the duty of the Army Medical Corps, but it will have to be done. As plans are made to meet this emergency let us hope that such plans will include prompt attention to this group of lightly wounded. I was delighted to hear from a member of our staff who is now working in London that separate units have been established for this very purpose.

CONCLUSION

I feel strongly that the care of the lightly wounded as I saw it in France was greatly neglected. I sincerely hope that this will not occur when we have to meet the problem again. God grant that we do not have to, but should it come let us be ready for it.

and increases the intrapericardial pressure if denied free egress. Compression of the great veins at the base of the heart backs up the venous inflow and compensatory increase in venous pressure results. The blood pressure falls and the systolic and diastolic pressures tend to approximate each other because the heart is handling less blood. When the increasing venous pressure cannot overcome the intrapericardial pressure, circulatory arrest occurs. As little as 200 cubic centimeters of blood may cause fatal tamponade quickly if it escapes rapidly into the pericardium. On the other hand, a slow leak, as from an ice pick wound, may produce fatal tamponade several days later, as in Case A9. If the opening in the pericardium is of such size and location as to permit free and unimpeded flow to the exterior or into the pleura, tamponade does not occur but fatal hemorrhage ensues unless it is checked. As might be expected, many patients with large cardiac wounds and massive hemorrhage succumb before surgical aid is available. Death may occur in the hospital during the few minutes that it takes to make the diagnosis and start operation, even with the best organization.

Often the two conditions, tamponade and hemorrhage, occur simultaneously when the hole in the pericardium allows large quantities of blood to escape but not fast enough to decompress the rapidly filling pericardium. Occasionally, tamponade and extrapericardial bleeding occur alternately. In 2 cases in our series, increasing tamponade was evident until the intrapericardial pressure apparently reached the point where it could force open the communicating wound into the pleura. Spontaneous drainage into the pleura relieved the symptoms of tamponade, which recurred however, within a few minutes. Several such cycles were observed and, in 1 patient, could be brought about by changing position, which probably opened the wound in the pericardium. In a small proportion of cases, bleeding from the heart is small in amount and ceases spontaneously. If the pericardial opening in such cases allows decompression, recovery will ensue without surgical treatment.

Cerebral damage may occur as a result of emboli thrown off from mural thrombi in the

cardiac chambers, or as a result of cerebral anoxemia produced by neglected tamponade. The intracranial pressure closely parallels the high venous pressure and, in Case A1 of our series, reached 400 millimeters of spinal fluid. This high intracranial pressure and coexisting low blood pressure reduce the flow of blood through the brain so that harmful and even fatal cerebral anoxemia may occur. Extrapericardial hematomas may produce enough compression of the heart to give rise to tamponade. Such hematomas most frequently arise from division of the internal mammary artery, as in Cases C1, C4, and C7.

DIAGNOSIS

The diagnosis depends primarily upon an alert house staff keeping in mind the possibility of cardiac injury in every case of wound of the chest, no matter how trivial. This is especially true when the evidence of shock is out of proportion to the apparent severity of the wound or loss of blood. Acute alcoholism often clouds the picture and, in our series, was present in all but 2 cases. When acute tamponade is present, Beck's triad of acute cardiac compression is found. This triad consists of (a) falling arterial pressure, (b) rising venous pressure, and (c) small, quiet heart. (4) The patient appears to be in shock. The blood pressure, and particularly the pulse pressure, are low or unobtainable. The pulse is weak but not so rapid as might be expected unless there is considerable hemorrhage. Heart sounds are weak and distant. Increased venous pressure is evidenced by distended neck veins and cyanosis is often present. Direct measurement of the venous pressure at the elbow, by use of a water spinal manometer filled with 2½ per cent sodium citrate or normal saline solution, shows an increase often to 250 millimeters or more. Delirium, stupor, unconsciousness, or hemiplegia may occur, due to alcoholism, cerebral anoxemia, or emboli. Fluoroscopy is of the greatest value in diagnosis and clearly shows diminished or absent pulsation of the heart shadow. If available, a roentgen kymogram is of great aid.

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PENETRATING WOUNDS OF THE HEART AND PERICARDIUM

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WOUNDS of the heart were recognized in Homeric times, but none was successfully sutured until 1896. The history of the intervening 2500 or 30 years of speculation, experiment, and trial has been related by Ricketts, Cutler and Beck and by Elkin (10) and need not be repeated here. Since the first successful operation by Rehn in 1896 the recognition and treatment of this condition has become more frequent, until today hardly a month goes by without the report of successful suture of a cardiac wound. Review of the many single case reports in the literature probably gives an optimistic view of the mortality since unsuccessful single cases are seldom reported. The results of a questionnaire sent out by Bigger (5) to the members of the American Association for Thoracic Surgery, the American Surgical Association, and the Southern Surgical Association showed a mortality of approximately 50 per cent in 141 patients. Bigger (6) and Elkin (10) have reported series of 25 and 38 cases with mortality of 36 and 41 per cent in those cases which presented an opportunity for diagnosis and treatment. Prior to 1933 3 wounds of the heart were recognized and operated upon at the Louisville City Hospital by Sherrill in 1913 Hill (7) in 1926 and Cox in 1927 the last case having successful termination. Since 1933 from 2 to 8 cases have been seen yearly. This large number probably indicates not so much an increase in the number of heart wounds as it does an increased awareness of and interest in, the condition, since the diagnosis depends primarily upon keeping in mind the possibility of cardiac injury in every case of wound of the thorax. Elkin states that at Emory University 2 per cent of the pene-

trating wounds of the chest injured the heart. In Bigger's experience 0.1 per cent of admissions to his surgical service in Richmond are wounds of the heart. These figures closely approximate our findings at the Louisville City Hospital.

PATHOLOGY

Wounds of the heart may of course, be caused by any sharp instrument or projectile. The weapon and the type of wound vary according to the local customs of the civilian population, or current military practice. In our experience, the knife, pistol and ice pick have been the most frequent weapons. A weapon or projectile may reach the heart from an entrance anywhere on the chest or even the upper abdomen. In most cases, however the wound of entrance is between the second and seventh left costal cartilages anteriorly usually traversing the left pleura. Occasionally the heart is reached from a wound of the posterior thorax. The right ventricle is the most frequently injured on account of its anterior position. Next in order of frequency are the left ventricle, the auricles, and the intrapericardial portions of the great vessels. Sucking wounds of the pleura are not uncommon. Injury to the peripheral portion of the lungs is frequent but usually of little moment.

Wounds of the heart may or may not penetrate the cavities. Bleeding from coronary vessels and the heart muscle, while not so profuse as when the chambers are opened, is surprisingly brisk and may be rapidly fatal. The consequences of cardiac hemorrhage are due in the main, to tamponade and exsanguination. The alternative between tamponade and exsanguination depends upon the relative flow capacities of the cardiac wound and the opening in the pericardium. Blood escaping from the heart fills the pericardium

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and increases the intrapericardial pressure if denied free egress. Compression of the great veins at the base of the heart backs up the venous inflow and compensatory increase in venous pressure results. The blood pressure falls and the systolic and diastolic pressures tend to approximate each other because the heart is handling less blood. When the increasing venous pressure cannot overcome the intrapericardial pressure, circulatory arrest occurs. As little as 200 cubic centimeters of blood may cause fatal tamponade quickly if it escapes rapidly into the pericardium. On the other hand, a slow leak, as from an ice pick wound, may produce fatal tamponade several days later, as in Case 19. If the opening in the pericardium is of such size and location as to permit free and unimpeded flow to the exterior or into the pleura, tamponade does not occur but fatal hemorrhage ensues unless it is checked. As might be expected, many patients with large cardiac wounds and massive hemorrhage succumb before surgical aid is available. Death may occur in the hospital during the few minutes that it takes to make the diagnosis and start operation, even with the best organization.

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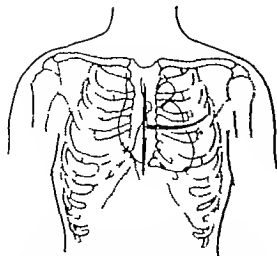


Fig. 1. A transverse incision is made over the interspaces where the wound of entrance is located and the wound of entrance is excised with the incision. The vertical portions upward, downward or both is added later if necessary. Incision is always made on the left, except when the wound of entrance is far to the right.

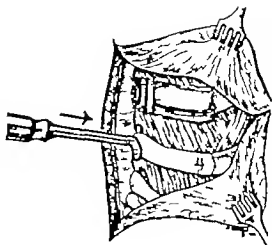


Fig. 2. After clearing of soft parts from the costal cartilage, Doyen's respiratory is introduced about the cartilage, close to the sternum, and pushed gently in lateral direction. This strips the soft tissues from the rib and enables one to do rapid resection without injuring the pleura or the internal mammary artery piece, if correctly inserted, the instrument invariably enters the proper plane of cleavage superficial to the pleura.

wound of the heart may be more difficult, but the indications for immediate operative intervention are clear and imperative. Bleeding from the parenchyma of the lung in wounds of the thorax may be massive but is slow and seldom requires operative hemostasis. On the other hand free bleeding from the heart, great vessels internal mammary or intercostal arteries is fast and profuse. Rapidly progressive shock is present early and death may quickly ensue unless hemorrhage is checked. We believe, therefore, that in the presence of increasing hemothorax and rapidly progressive fall in blood pressure, particularly with a precordial wound, exploration should be carried out at once, for even though the heart be intact, the arrest of hemorrhage from other structures is imperative.

TREATMENT

Once the diagnosis and the decision to intervene are made operation should be immediate and no preoperative treatment for shock or other condition should be allowed to delay operation. Intravenous fluids, particularly blood, should be administered when hemorrhage has occurred but are of little value preoperatively in case of tamponade. Morphine

is used sparingly particularly in the presence of alcoholism and tamponade because of its effect upon an already depressed respiratory center. Aspiration of the pericardium as recommended by Bigler may be a lifesaving measure to tide the patient over while preparations are made for operation. Speed, but not haste, in preparing for operation is essential. Every large general hospital should have available at all times a sterile setup of instruments and linens, and the operating room, with at least one nurse and orderly in attendance, should be open 24 hours a day. No short cuts should be taken however in the scrub up of the team or the preparation of the field of operation. Undue haste here may be followed by empyema and pericarditis later. We have had no deaths from infection and believe that this is the result of the same careful preparation as is used for any elective procedure.

A minimum of inhalation anesthesia is advisable, although oxygen under positive pressure is usually necessary on account of

the open pleura. The soporific effects of shock, tamponade, or alcoholism are generally present, but deeper anesthesia is often necessary after the release of tamponade. Our preference is for intercostal novocain block, usually of the third to sixth nerves, supplemented by oxygen and the minimum of nitrous oxide.

The incision should be one which permits rapid and adequate exposure of the heart and is made to the left of the sternum unless the wound of entrance is far to the right. This is best accomplished by a generous transverse incision over the interspace in which the wound is located. The wound of entrance is excised with this incision. The transverse incision may be joined, when necessary, by a vertical incision over the sternum (Fig 1). The costal cartilages above and below the incision are exposed and resected with about 1 inch of rib, by the method described by Meyer. "Previously, subperiosteal resection of the ribs with a pleura often as thin as a spider's web, was a task, especially in a moribund patient, extremely trying. The operation must be carried out with meticulous care and yet with great rapidity. However, one can resect the ribs in a few seconds and the steps of the operation are simple and the pleura is not opened or injured. The sternum must be exposed more than usual. The raspatory is introduced quite close to the sternum at the cartilaginous portion of the rib. This takes only a few seconds. Fat lies beneath, loose, and can readily be pushed aside. Here the Doyen raspatory is brought into play.

"It is inserted medial to the internal mammary artery and when pushed further in a lateral direction we resect the ribs extrapleurally as far as necessary and without danger to the pleura, because in this layer, the pleura is surprisingly easy to remove" (Fig 2). The internal mammary vessels are ligated and divided and the triangularis muscle and endothoracic fascia opened. The pleura is reflected from the pericardium by blunt dissection, beginning at the lower angle of the wound. Often this may be done by inserting the finger between the pericardium and pleura in the triangle of safety where the pericardium is uncovered by pleura. The

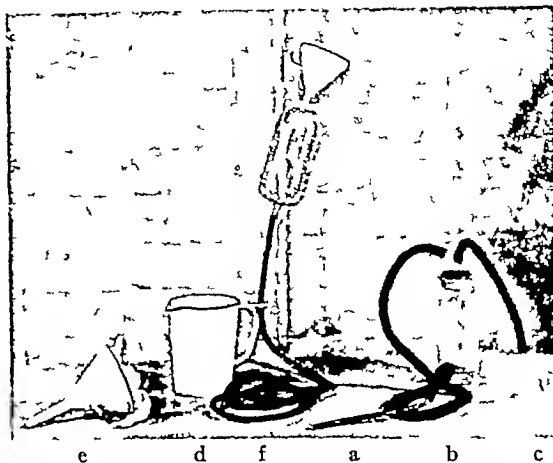


Fig 3 Autotransfusion outfit used in all cases of hemorrhage into body cavities. *a*, Pool suction tip, *b*, 500 cubic centimeter bottle with two-hole stopper containing citrate solution, *c*, tube running to operating room suction, *d*, 1000 cubic centimeter graduate, *e*, funnel with gauze filter, *f*, intravenous outfit with Murphy drip.

finger is then swept cephalad, easily separating the two structures. As much as necessary of the sternum is rongeured away. If additional exposure seems advisable on account of an oblique wound, the vertical limb is added to the incision upward, downward, or both, turning back triangular flaps which allow the removal of additional cartilages. If tamponade is present, the blood-filled pericardium will be tense, blue, and quiet. If the opening in the pericardium is large, it may usually be exposed and is best enlarged with the least damage to the heart, by gently but firmly spreading it with the fingers. If no opening is seen, the pericardium is nicked carefully after lifting it with forceps or stay sutures and this opening spread as above.

Clots are quickly scooped out of the pericardium with the fingers and liquid blood removed by suction into the autotransfusion outfit (Fig 3). With release of the tamponade the force and rate of the heart beat increase and bleeding becomes profuse, so that continuous suction is used from now on until the heart has been sutured.

Unless the wound is immediately visible and easily accessible, it is best to ignore the bleeding and insert a fine silk traction suture into the apex as advocated by Beck (2). There is nothing more disconcerting than to hold in

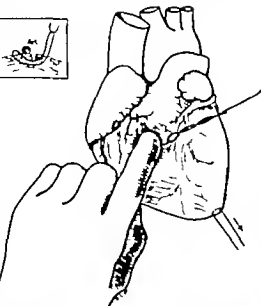


Fig. 4. Traction suture at apex, steady heart. While a silk suture is being passed under finger which has been placed over the wound. Inset shows method of inserting mattress suture to hold coronary vessel closed when wound is made to vessel.

One's hand a writhing jumping heart and vainly attempt to find a wound deep in a swirling whirlpool of blood. The insertion of a traction suture converts this stage of the operation from futile blundering into an orderly process. The traction suture steadies the jumping organ so that a finger may be placed over the opening temporarily to staunch the flow. A word of warning to those inexperienced in cardiac surgery is necessary at this point. If held rigidly the traction suture cuts through the myocardium with each systolic contraction. The hand holding the suture must therefore relax elastically with each beat, steadying but not fixing the heart. The finger must be placed over but not into the wound. One's natural tendency to insert the finger as a cork will only result in further laceration of the myocardium.

With the finger over the wound as temporary patch, a fine silk suture threaded on a French eye needle is inserted across the wound beneath the finger (Fig. 4). Slight traction on this suture holds the wound closed after the finger is removed and allows other

necessary sutures to be inserted. None of these sutures must be so deep as to penetrate the endocardium, on account of the increased risk of mural thrombi. They should be tied only tight enough to give hemostasis and must avoid strangulation of the muscle. Injured coronary vessels may be covered with a small patch of pectoral muscle (3) if the vessel is not completely severed. Complete division of large coronary arteries requires ligation by suture. Never attempt to grasp a bleeding coronary vessel with a hemostat. The closure of wounds close to large coronary vessels may present a problem. In Case A14 death resulted from occlusion of a large coronary vessel by the suture. This may be avoided easily by an "on-end" mattress suture beneath the vessel, as shown in Figure 4 insert.

If the wound is on the right or posterior portion of the ventricles, it may usually be exposed by appropriate traction on the suture at the apex. If necessary additional traction sutures well up on the ventricle may be used to rotate the heart to bring posterior wounds into view (Fig. 5).

Hemorrhage from wounds of the auricles and great vessels may be controlled temporarily by a soft clamp such as the Trendelenberg artery clip or the Horsley arterio-venous fistula clamp, or even with ordinary hemostats prior to the placing of sutures.

The blood collected in the autotransfusion bottles should, by now be running into the patient's veins. Any remaining blood in the pericardium and pleura is thoroughly sucked out for retransfusion. Autotransfusion in amounts up to 2500 cubic centimeters has been used in 14 of our cases. With the use of the apparatus illustrated it is a simple rapid procedure which is often life saving.

If there is already a free opening between the pericardium and pleura, this is left open and enlarged if necessary to allow adequate postoperative decompression of the pericardium into the pleura (11). This permits drainage of any remaining blood, as well as the increased pericardial fluid, which occurs after any operation upon the heart. Drainage to the exterior presents a real danger of infection as the draining fluid is sucked in and out of the drainage tract with each respiration.

The anterior pericardium is closed loosely with interrupted fine silk sutures. Tight closure is unnecessary and may be impossible or even harmful because of the cardiac dilatation which frequently occurs in these cases (1, 10). Soft tissues of the thoracic wall are closed firmly in layers with interrupted fine silk and the wound sealed with silver foil, after reinflation of the left lung by carefully applied positive pressure.

Recently, we have implanted up to 5 grams of powdered sulfanilamide or sulfathiazol into the pericardium and pleura before closure, as these wounds are all potentially infected.

Operation may sometimes be avoided in patients who have only mild tamponade and who do not have progressive intrapleural hemorrhage. These patients should, however, remain in the hospital and be confined strictly to bed until all danger of recurrent tamponade has passed. Frequently repeated observations of blood pressure, pulse, and venous pressure should be made, as well as daily fluoroscopic examination, since late tamponade may occur as in Cases A3, A9, A27. If tamponade is serious enough to require aspiration, as advocated by Bigger, open operation with wound suture and drainage of the pericardium into pleura is the treatment of choice.

POSTOPERATIVE TREATMENT

The patient is placed in an oxygen tent immediately after operation and is left there until his respiratory rate returns to normal. Fowler's position is usually the most comfortable and assists respiration. If shock has not been relieved by operation and autotransfusion, additional blood or plasma are indicated. Sufficient morphine should be administered to allay pain and restlessness, but not to depress respiration. Any remaining air and blood in the pleural cavity should be removed by thoracentesis to keep the lung expanded. This may be repeated at intervals as fluid reaccumulates, due to the irritating effect of blood on the serosa of the pericardium and pleura. The use of heparin, as suggested by Bigger, may be advisable, particularly when the weapon has pierced the endocardium. This may prevent deaths from embolism, such as occurred in Case A21.

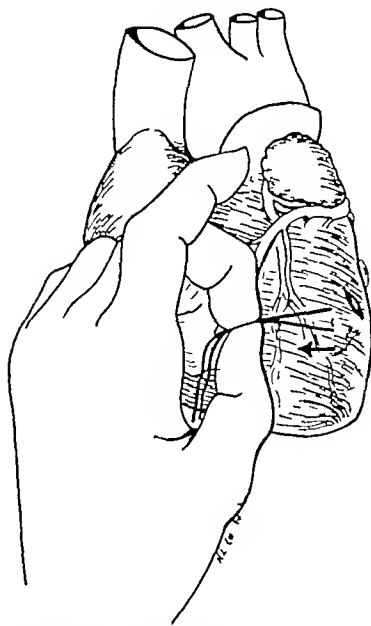


Fig 5 Showing use of additional traction suture for rotating heart in either direction. Several such sutures may be used.

PROGNOSIS

The prognosis of wounds of the heart depends largely upon the character of the wound and the rapidity with which treatment is initiated. Undoubtedly, some patients die immediately because of disruption of the conducting mechanism of the heart. Many with large wounds succumb rapidly from hemorrhage before they can be transported to the hospital. This is particularly true of gunshot injuries with wounds of entrance and exit, often involving more than one chamber of the heart, as well as important extrapericardial structures. However, at least half the cases of massive hemorrhage and almost all the cases of tamponade, survive for an hour which, except in rural districts, should be time for transportation, diagnosis, and treatment. All patients, who died in the Louisville City Hospital before or during operation, were cases of hemorrhage, except 2 deaths from tamponade and 1 death on the table following occlusion of a major coronary artery. In those patients who survived operation, the most frequent fatal complication has been cerebral damage. This may be due to em-

bolism as in Case A21 or neglected tamponade and resultant cerebral anoxemia as in Cases A1, A4, A12 and A18. In those patients who lived the symptoms and signs of cerebral injury have disappeared spontaneously within a few months without leaving residual damage. No cases of fatal infection have been observed. It is our opinion that infection is most often caused by undue excitement and haste in preparation or by drainage of the pericardium externally. Clinical cardiac disability has been uniformly absent after operation and there has been no indication of reduced cardiac reserve. Electrocardiograph changes are usual following wounds of the heart, and vary from minor irregularities of the T wave to the typical picture of major coronary occlusion, as shown in Case A24. These abnormalities improve and sometimes even disappear within a few months. A detailed analysis of these changes is to be reported at a later time.

CASES

During the last 8 years, 47 patients with presumed or proved wounds of the heart have been admitted to the Louisville City Hospital. Fourteen of these have been reported previously in detail (1, 12, 13). Operations were performed by the senior author and, under his guidance, by the following resident surgeons at the Louisville City Hospital: J. M. Blayer, E. M. Driscoll, H. G. Saam, V. A. Badertscher, C. M. Bernhard, C. M. Schroeder, C. H. Maguire and E. S. Strode. In 7 cases the presumption that the heart was wounded was not borne out, but interesting cardiac aspects justify their inclusion in this report. Death occurred in 13 cases within 30 minutes of admission before operation could be started. In no case was operation delayed or refused, because of the moribund condition of the patient. Five of the patients operated upon were on the table within 30 minutes of admission, having been brought directly from the accident room. In the 27 cases which presented an opportunity for diagnosis and treatment, there were 7 deaths, a mortality of 25.9 per cent (Table I). Five were treated conservatively with 1 death. This patient refused to stay in the hospital and died of

tamponade on the eleventh day. Twenty-two patients were operated upon, with 6 deaths. Two of these deaths were due to hemorrhage, 1 on the table and 1 30 minutes after operation. One died on the table following ligation of a major coronary artery, and there were 3 deaths 18 hours, 48 hours, and 5 days after operation, due to cerebral complications. Our mortality has decreased with experience so that in the last 13 cases there has been but 1 death.

CASE A. W. M. A 3283 colored male, aged 30 years, with a ice pick wound in the left anterior axillary line in the sixth interspace, seen in marked shock. No blood pressure was discernible, heart sounds were distant, pulse weak and 60 per minute. The patient had lacerated scalp and other ice pick wounds and was observed for 8 hours and then prepared for subtemporal decompression because of hemiplegia and unconsciousness that had developed. Spinal fluid pressure 25-400 mm. Hg. Fluorocopy showed 100 round heart shadow. The pericardium was explored and ice pick wound of left ventricle with tamponade found. The patient never regained consciousness and died 8 hours after operation, with cerebral manifestations and terminal fever of 103° (3).

CASE A. J. D. 429133 colored male, aged 22 years, was sent directly from the emergency room to the operating room. There was a knife wound in the left anterior axillary line in the third interspace. The patient was in marked shock, no blood pressure obtainable. Exploration revealed 1 by 1/2-inch laceration in the left ventricle and 3500 cubic centimeters of blood in the left pleural cavity. He died on the operating table from exsanguination (3).

CASE A3. W. J. A3 773 colored male, aged 35 years, was seen with a stab wound in the seventh interspace, 2 centimeters to the left of the sternum. Blood pressure was 98/70. Roentgenogram showed slight enlargement of heart shadow. On the second day the patient collapsed on getting out of bed and went into extreme shock; he recovered slowly. The same thing was repeated on the fourth day. He was discharged on the twelfth day and readmitted 6 days later with edema of scrotum and legs, distant heart sounds and enlarged shadow. Uneventful recovery took place (1).

CASE A4. V. H. 34 95 colored male, aged 38 years, with a stab wound in the left anterior axillary line, the level of the sixth rib was admitted in marked shock. He improved under observation. X-ray picture showed wide heart shadow. Patient was observed for 4 hours and then exploration operation carried out because of development of paradoxical pulse and right-sided twitches. Laceration of posterolateral wall of left ventricle was found and sutured. Recovery took place. Patient discharged on the thirty-fifth day (1).

CASE A5 W C, 34388, white male, aged 11 years, with .22 caliber rifle wound in fourth interspace 3 centimeters to the right of the sternum was seen in marked shock. No blood pressure was obtainable, pulse was 70, heart sounds distant. Fluoroscopy revealed slight enlargement of the heart shadow. A laceration in the upper lateral portion of the right ventricle was closed. Patient was discharged on the thirty-fifth day (13).

CASE A6 J S, 38543, colored male, aged 35 years, was stabbed in the right chest with scissors. Sucking wound was present in the fourth interspace. Blood pressure varied greatly on observation. Venous pressure was 150 millimeters of water. X-ray film of chest revealed hemopneumopericardium with a definite fluid level. His hospital course was uneventful and patient was discharged on seventeenth day (13).

CASE A7 C T, 43640, colored male, aged 26 years, with gunshot wound in the fifth interspace in the left anterior axillary line was seen in marked shock. No blood pressure was obtainable, heart sounds were distant, pulse 80 per minute. Wound in the lower portion of the left ventricle was found and sutured. No wound of exit was found. Recovery was uneventful. Patient was discharged on the forty-second day. X-ray film showed bullet in right iliac artery. Distal pulsation was absent but circulation adequate (12).

CASE A8 T R, 44460, colored male, aged 17 years, with laceration of chest, beginning in left fifth interspace in midclavicular line and extending across sternum to 2 centimeters on right was in moderate shock. Blood pressure was 74/50, pulse, 100 per minute. Patient was operated upon within 45 minutes after admission. Laceration of right auricle was found and sutured, but patient had lost too much blood and died 30 minutes after operation (12).

CASE A9 A C, 44937, white female, aged 29 years, was stabbed repeatedly with an ice pick. There was subcutaneous emphysema throughout most of the chest wall. Fluoroscopy showed enlarged cardiac shadow with decrease in pulsation. Patient refused to stay in hospital and died 11 days after injury while straining at stool. Autopsy revealed a puncture wound of the left auricle that had apparently oozed slowly and caused fatal tamponade (12).

CASE A10 E H, 43909, colored male, aged 48 years, with 4 stab wounds in the third interspace on the left was in marked shock. Blood pressure was 46/40, heart sounds, distant, pulse, paradoxical and 80 per minute. Fluoroscopy showed enlarged heart shadow. Three lacerations in the left ventricle were sutured, and recovery was uneventful. Patient was discharged on the thirty-fourth day (12).

CASE A11 F W, A52994, colored female, aged 28 years, was seen with stab wound in the sixth interspace just to left of sternum. Neck and arm veins were distended. Patient was in moderate shock, blood pressure was 80/60, heart sounds,

muffled, pulse paradoxical and 100 per minute. Laceration of right ventricle sutured. Recovery was uneventful. Patient was discharged on the twenty-sixth day.

CASE A12 L R, 1623, white male, aged 27 years, was seen with 6 centimeter laceration in the fourth interspace in the precordium. Heart sounds were distant, blood pressure, 40/0, pulse, 80 per minute. Neck veins were distended. Internal mammary and right auricle were lacerated. They were sutured successfully but patient remained unconscious and died at end of 48 hours with a terminal fever of 108 degrees, due either to cerebral anoxemia or post-operative heat stroke. Autopsy showed the heart wounds to be sutured satisfactorily.

CASE A13 E C, 2322, colored male, aged 23 years, with stab wound in right fourth interspace 4 centimeters from sternum was seen in marked shock. Blood pressure was unobtainable, heart sounds, quite distant, pulse, weak and recorded as 40 per minute. Laceration of right ventricle on the upper anterior aspect found and sutured. Recovery was uneventful. It is interesting, in this case, that there was moderate bleeding to the outside and when operation was carried out, it was found that there was obliteration of both pleural cavities. Patient was discharged on the twenty-sixth day.

CASE A14 M L, 26018, colored female, aged 20 years, with stab wound in fourth interspace 2 centimeters to left of sternum was seen in marked shock. Blood pressure was unobtainable, heart sounds, distant, pulse, weak, 60 per minute. Laceration of right ventricle was adjacent to the descending coronary artery. Coronary vessels were tied during suture of the wound. Typical acute cardiac dilatation and death on the table followed (1).

CASE A15 C B, 26804, colored male, aged 34 years, with transverse laceration that involved the seventh and eighth costal cartilages and nicked the sternum was seen in marked shock. Blood pressure was unobtainable, no radial pulse palpable, heart sounds quite distant, 100 per minute. Laceration of the midportion of the right ventricle was sutured. Recovery was uneventful. Patient was discharged on the eighteenth day.

CASE A16 B A, 3088, colored male, aged 34 years, with stab wound in the sixth interspace just to the left of the sternum was seen in moderate shock. Blood pressure was 94/64, pulse, 96 per minute, neck veins, distended, venous pressure, 250 millimeters of water, heart sounds, muffled. Fluoroscopy revealed enlarged nonpulsatile shadow. Laceration of tip of the anterior surface of the right ventricle was sutured. Recovery was uneventful. Patient was discharged on the eighteenth day.

CASE A17 E G, 29910, white female, aged 36 years, had received three ice pick wounds in the third interspace just to right of sternum, also a wound in the posterior chest just to the left of the vertebrae. Blood pressure was 70/50, pulse, 120 per minute, neck veins, distended, venous pressure, 200 millimeters of water, heart sounds, distant, patient

bolism as in Case A21 or neglected tamponade and resultant cerebral anoxemia, as in Cases A1 A4 A12 and A18. In those patients who lived the symptoms and signs of cerebral injury have disappeared spontaneously within a few months without leaving residual damage. No cases of fatal infection have been observed. It is our opinion that infection is most often caused by undue excitement and haste in preparation or by drainage of the pericardium externally. Clinical cardiac disability has been uniformly absent after operation and there has been no indication of reduced cardiac reserve. Electrocardiograph changes are usual following wounds of the heart, and vary from minor irregularities of the T wave to the typical picture of major coronary occlusion as shown in Case A24. These abnormalities improve and sometimes even disappear within a few months. A detailed analysis of these changes is to be reported at a later time.

CASES

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tamponade on the eleventh day. Two of these deaths were on the table and 1 soon after admission. One died on the table of a major coronary artery aneurysm 18 hours, 48 hours after operation, due to cerebral anoxemia. Mortality has decreased so that in the last 13 cases there was 1 death.

CASE A1. W. M. A18 53 years, with ice pick wound of the left chest, auxiliary line in the sixth intercostal space, marked shock. No blood pressure. Heart sounds were distant, pulmonary clear. The patient had 12 other ice pick wounds and was obtunded and then prepared for subtemporal craniotomy because of hemiplegia and aphasia. Spinal fluid pressure 18 mm. Hg. Fluoroscopy showed shadow of the pericardium was 2 cm. from the left ventricle. 15th minute after operation 15th minute patient never regained consciousness. 15th minute terminal fever of 103° (3).

CASE A2. J. D. A20433 colored, was sent directly from the accident room to the operating room. There was a 1/2 inch left anterior auxiliary line in the third intercostal space, marked shock, no blood pressure. Exploration revealed laceration of the left ventricle and 1/2 inch of blood in the left pleural space. On the operating table from exsanguination.

CASE A3. W. J. A31773 colored, 35 years, was sent with stab wound of the left chest, 1/2 inch, 1/2 inch from the left. Blood pressure was 95/70. Roentgen showed enlargement of heart shadow. Day the patient collapsed on getting up. Went into extreme shock. He recovered same thing was repeated on the fourth day. Discharged on the 15th day. Had no later with edema of scrotum and legs. Sounds and enlarged shadow. Unfavorable took place (2).

CASE A4. V. H. 34 95 colored, 35 years, with stab wound of the left chest at the level of the sixth rib, 1/2 inch, marked shock. He improved under X-ray picture showed wide heart shadow was observed for 22 hours and the operation carried out because of deep paradoxical pulse and right-sided twelfth rib fracture of posterolateral. All of left lung found and sutured. Recovery took place. Was discharged on the thirty-fifth day.

CASE A5 W C, 34388, white male, aged 11 years, with 22 caliber rifle wound in fourth interspace 3 centimeters to the right of the sternum was seen in marked shock. No blood pressure was obtainable, pulse was 70, heart sounds distant. Fluoroscopy revealed slight enlargement of the heart shadow. A laceration in the upper lateral portion of the right ventricle was closed. Patient was discharged on the thirty-fifth day (13).

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CASE A11 F W, 452004, colored female, aged 28 years, was seen with stab wound in the sixth interspace just to left of sternum. Neck and arm veins were distended. Patient was in moderate shock, blood pressure was 80/60, heart sounds,

muffled, pulse paradoxical and 100 per minute. Laceration of right ventricle sutured. Recovery was uneventful. Patient was discharged on the twenty-sixth day.

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CASE A16 B A, 3088, colored male, aged 34 years, with stab wound in the sixth interspace just to the left of the sternum was seen in moderate shock. Blood pressure was 94/64, pulse, 96 per minute, neck veins, distended, venous pressure, 250 millimeters of water, heart sounds, muffled. Fluoroscopy revealed enlarged nonpulsatile shadow. Laceration of tip of the anterior surface of the right ventricle was sutured. Recovery was uneventful. Patient was discharged on the eighteenth day.

CASE A17 E G, 29910, white female, aged 36 years, had received three ice pick wounds in the third interspace just to right of sternum, also a wound in the posterior chest just to the left of the vertebrae. Blood pressure was 70/50, pulse, 120 per minute, neck veins, distended, venous pressure, 200 millimeters of water, heart sounds, distant, patient

In mild shock. Fluoroscopy revealed enlarged nonpulsatile shadow. Wound in anterior portion of the sternum just above the valves was closed with silk suture. Recovery was uneventful. Patient was discharged on the fifteenth day.

CASE A 8. L. S. 385 colored male, aged 3 years, walked into the emergency room and collapsed. He was in marked shock. Patient had received stab wound in the fourth interspace 4 centimeters to the left of the sternum. Blood pressure was 78/60 pulse, 20 per minute. There was slight venous distention. Venous pressure, 100 millimeters of water, heart sounds of fair quality. Fluoroscopy showed large nonpulsatile shadow and kymogram limitation of ventricular excursion. There was laceration in the left ventricle with hematoma over the anterior descending branch of the left coronary vessels. Infection of skin flaps developed and then osteomyelitis of the ends of the fourth and fifth ribs. There also developed a left facial weakness. Patient was discharged in 37 days with both these conditions cleared up.

CASE A 9. S. W. 586, colored male, aged 4 years, had received stab wound just to the left of the costiform cartilage. Patient was in marked shock. Blood pressure, 44/0 muffled irregular cardiac sounds, pulse, 60 per minute, paradoxical in type. Neck veins were distended, and venous pressure 200 and 250 millimeters of water on successive readings. Fluoroscopy showed enlarged nonpulsatile shadow. Laceration of right ventricle on the anterior inferior aspect was sutured. Recovery as uneventful. Patient was discharged on the fifteenth day.

CASE A 20. A. B. L. 7704 colored male, aged 7 years, with stab wound in the fifth interspace just beneath the left pectoral fold was seen in profound shock. Blood pressure was 40/30 neck veins were distended venous pressure as 80 millimeters of water heart sounds distant pulse 60 per minute. Fluoroscopy revealed large nonpulsatile shadow. Laceration of the left ventricle 3 centimeters in length was sutured. Recovery was uneventful. Patient was discharged on the fifteenth day.

CASE A 1. J. W. H. 80030, colored male, aged 3 years, had received stab wound in the fifth interspace in left anterior axillary line. Blood pressure was 60/40 pulse 60 per minute. Neck veins were distended, venous pressure was 100 millimeters of water heart sounds distant with paradoxical pulse. Fluoroscopy showed enlarged nonpulsatile shadow. Laceration of lateral side of left ventricle was sutured. Patient died on the fifth day with complete right-sided hemiplegia. A autopsy showed large mural thrombus at the site of wound in endocardium and an embolus plugged left middle cerebral artery.

CASE A 2. L. J. 80755 colored male aged 36 years had received ice pick wound in the third interspace 5 centimeters to the left of the sternum and other wounds slightly below and lateral to this one. Patient was in shock. Blood pressure was 60/5 pulse 84 per minute. Heart sounds were distant there was slight venous distention venous

pressure was 11 millimeters of water. Fluoroscopy showed enlarged nonpulsatile shadow. Exploration revealed tamponade and lacerations of the arch of the aorta. Recovery was uneventful. Patient was discharged on the thirteenth day.

CASE A 3. L. H. 80854, colored male aged 20 years with gunshot wound of left chest in the fourth interspace was seen in marked shock. Pressure was 40/0 pulse, 70 per minute neck veins, slightly distended venous pressure 80 millimeters of water no audible heart sounds. Fluoroscopy revealed wide nonpulsatile shadow and the bullet in the right lung. Exploration disclosed a fractured sternum and tamponade. The bullet had driven fragment of sternum into the wall of the right ventricle. Recovery was uneventful. Patient was discharged on the fourteenth day.

CASE A 24. J. D. H. 5106 colored male, aged 10 years, with stab wound in the fourth interspace 4 centimeters to the left of sternum was seen in marked shock. Blood pressure was unobtainable pulse 80 per minute. Patient was taken direct to operating room without fluoroscopy or venous pressure readings. A laceration of the left atrioventricular groove 4 centimeters in length which had severed the anterior descending branch of the left coronary artery was sutured. Recovery as uneventful. Patient was discharged on the thirty eighth day. Electrocardiogram showed typical anterior coronary block. This has improved to the present date.

CASE A 25. J. C. 804 colored male, aged 7 years, as admitted 7 hours after having been stabbed in the sixth interspace just posterior to anterior axillary line. Patient complained of occasional precordial pain, slight dyspnea, moderate venous distention. Venous pressure was 50 to 60 millimeters of water. Fluoroscopy showed wide cardiac shadow and kymogram showed decreased ventricular excursion. Patient was comfortable with exception of slight dyspnea. He was discharged on the ninth day.

CASE A 26. W. H. 5765 hit male aged 25 years with stab wound 1 centimeter medial and below left nipple was seen in moderate shock. Blood pressure was 80/4 pulse 100 and rapid heart sounds faint. Venous pressure as 60 millimeters of water. Fluoroscopy showed decreased pulsation. A hemothorax as present. Laceration of left ventricle 5 centimeters in length as sutured. Recovery was uneventful.

CASE A 27. J. T. 848 colored male, aged 5 years, was seen with stab wounds in left third interspace 4 centimeters from midsternal line and just below xyphoid at left costal margin. There was no shock. Blood pressure was 30/80 pulse 30. Venous pressure was 11 millimeters of water. Heart sounds were normal except for succussion splash. X-ray film showed hemo-pericardium. An operation was done. On the second day blood pressure was 86/60 and venous pressure 50 millimeters of water. Spontaneous improvement occurred, however and uneventful recovery ensued.

TABLE II

Case	Year	Sex	Age	Weapon	Time from admission to death	Location	Remarks
B	15	M	?	Knife	no data	R. V.	gross ch. hemothorax
B	1913	M		Postal	no data	R. V. and aorta	Hemothorax
B	1916	M	33	Knife	no data	L. V.	Hemothorax
	1917	M	24	Postal	On arrival	R. and L. V.	Hemothorax
B	1917	M	30	Knife	On arrival	L. V.	Tamponade and hemothorax
B	1917	M	24	Knife	On arrival	L. V.	Hemothorax
B	1917	M	25	Postal	On arrival	R. and L. V.	Hemothorax
B	1917	M	24	Knife	On arrival	Aorta	Hemothorax
B	1919	M	23	Knife	no data	L. V.	Tamponade
B	1920	M	41	Postal	no data	R. V.	Hemothorax
B	1921	M	44	Postal	On arrival	Aorta	Hemothorax
B	1921	M	30	Postal	On arrival	Pulmonary artery and L. V.	Hemothorax
B	1921	M	24	Postal	no data	R. and L. V.	Hemothorax

the fifth rib, 7 cc. thru the right of sternum. There was 2000 cubic centimeters of blood in pleural cavities pericardium was full and there was a wound through both ventricles.

CASE B5. S. W. B5450, colored male, aged 3 years with stab wound of the first interspace 1 centimeter to left of sternum, died on admission to emergency room. Autopsy revealed acute tamponade. Pericardial sac contained 200 cubic centimeters of blood. There were 600 cubic centimeters of blood in each pleural cavity. A laceration of the left ventricle near the atrioventricular groove was found.

CASE B6. T. J. B900, colored male, aged 24 years with stab wound of the sixth interspace 2.5 centimeters to left of sternum, died on admission to emergency room. Each pleural cavity contained 600 cubic centimeters of blood and pericardium was full. There was laceration of all of the left ventricle which extended into the interventricular septum.

CASE B7. C. S. B90063, colored male, aged 35 years with gunshot wound of the sixth rib 1 centimeter to left of sternum was dead on arrival. There was 400 cubic centimeters of blood in pericardium and approximately 600 cubic centimeters in each pleural cavity. There was through-and-through wound of the heart involving both ventricles and the septum.

CASE B8. J. S., 992, colored male, aged 24 years, with stab wound just below midportion of left clavicle, was dead on arrival. Both pleurae were full of blood, pericardium contained 60 cubic centimeters. There was a through-and-through laceration of the ascending aorta just above the valves.

CASE B9. D. McC. 78674, white male, aged 30 years, with stab wound of the fifth intercostal space 1/2 to left of sternum, arrived in emergency room

breathing but died by the time he reached the ward. Acute tamponade was present with 450 cubic centimeters of blood in pericardial sac and a 5 centimeter laceration in wall of right ventricle 2 centimeters from apex.

CASE B10. R. G. B5850, colored male, aged 43 years, had received gunshot wound of the sixth intercostal space 1 centimeter to left of sternum with wound of exit posteriorly 6 centimeters to left of midline at level of the twelfth rib. Patient expired in 15 minutes. There was wound of the right ventricle which was 3 centimeters from the apex and 600 cubic centimeters of blood was in each pleural cavity.

CASE B11. L. B. B316, colored male, aged 41 years, with gunshot wound in anterior axillary line with wound of exit, was dead on arrival. There was laceration of the aorta 6 centimeters above the valves with 500 cubic centimeters of blood in pericardial sac, 500 cubic centimeters of blood in left pleural cavity and 700 cubic centimeters in the right.

CASE B12. L. E., B364, colored male, aged 30 years, with gunshot wound of the second interspace in left midclavicular line expired on arrival. There was a wound along the wall of the left ventricle and of the posterior wall of the pulmonary aorta. There was 500 cubic centimeters of blood in pericardium and 200 cubic centimeters of blood in each pleural cavity.

CASE B13. J. P. 37803, colored male, aged 4 years, had received gunshot wound of left sternal border in the fifth intercostal space. Heart sounds were distant. There was no palpable pulse; blood pressure was not discernible. Patient died in 15 minutes before prepared for operation. Through-and-through wound of both ventricles as present with hemothorax of 3000 cubic centimeters.

TABLE III

Case	Year	Sex	Age	Weapon	Result	Remarks
C1	1934	F	43	Knife	Lived	Venous pressure 250 extrapericardial hematoma
C2	1937	F	31	Pistol	Died	Wound of pericardium and diaphragm
C3	1937	M	25	Knife	Died	Internal mammary hemorrhage and hemothorax
C4	1937	M	9	Knife	Died	Internal mammary hemorrhage and extrapericardial hematoma
C5	1938	M	40	Knife	Lived	Acute cardiac dilatation
C6	1940	M	37	Pistol	Lived	Hemothorax
C7	1941	M	24	Pistol	Lived	Extrapericardial hematoma

Of the 7 cases in which the presumption of wound of the heart was not borne out at operation, 3 had tamponade due to the pressure of extrapericardial hematomas. In 2 there was massive intrapleural arterial hemorrhage and in 1 a wound of the pericardium and diaphragm but not of the heart. The most interesting of this group, Case C5, acute cardiac dilatation, relieved by pericardiotomy, has been discussed in detail by Badertscher (Table III).

CASE C1 H T, 38700, colored female, aged 43 years, with stab wound in the fourth interspace 5 centimeters to left of sternum was seen in moderate shock. Blood pressure was 68/20, pulse, 82 per minute, venous pressure, 250 millimeters of water. There was present a laceration of pericardium and about 100 cubic centimeters of blood in pericardium but no definite cardiac wound. However, there was a large extrapericardial hematoma from the internal mammary artery with pressure on the pericardium, causing tamponade. Course was uneventful. Patient was discharged on the twenty-fourth day.

CASE C2 E R, A59731, colored female, aged 31 years, had received pistol wound in the fifth interspace 1 centimeter to left of sternum, exit posteriorly in the seventh interspace. Patient was in marked shock. Blood pressure was unobtainable, heart sounds, distant, pulse, 100 per minute. Progress was progressively downward. Patient was taken to operating room after 2 hours, and exploration revealed an old adhesive pericarditis. The bullet had torn off some of the inferior part of the pericardium but there was no definite cardiac wound. The bullet had then perforated the diaphragm medial to the wound in the pericardium. Patient died 24 hours after operation, never coming out of shock.

CASE C3 C B, A59647, white male, aged 25 years, with sucking stab wound in left sixth interspace, was not in shock, but was explored because of position of the wound. Exploration revealed the left internal mammary artery severed but no heart wound. Patient died on the seventh day, apparently from secondary hemorrhage.

CASE C4 E R, A59647, colored male, aged 29 years, with stab wound in the third interspace 3

centimeters to right of sternum, was in marked shock. Blood pressure was 84/50, sounds were of good quality, there was slight venous distention. Exploration revealed the right internal mammary cut and 1000 cubic centimeters of blood in right chest. Patient died on the fourth day after operation.

CASE C5 W O S, 25733, colored male, aged 40 years, had received stab wound in the third interspace 2 centimeters to left of sternum. Blood pressure was 82/50, pulse, 70 per minute. Sounds were distant, slight venous distention was present, moderate shock. No pericardial wound was found but pericardium was quite tense and when it was cut the heart bulged into the opening and blood pressure came up to a normal level. Patient had an uneventful recovery and was discharged on the fifteenth day. (Discussed in detail by Badertscher.)

CASE C6 W H, 81802, white male, aged 32 years, with gunshot wound of the fifth interspace 5 centimeters to left of sternum, was seen in marked shock. Blood pressure was 40/20, pulse, 100 per minute, slight venous distention present. Fluoroscopic revealed no definite cardiac pulsation and the left chest was full of blood. No cardiac wound found on exploration. Left chest contained 1000 to 1500 cubic centimeters of blood. Patient signed out of hospital on the sixth day, but prior to that time his course had been uneventful.

CASE C7 S W, 14929, colored male, aged 24 years, with gunshot wound in the third interspace 5 centimeters to left of sternum, was seen in marked shock. Blood pressure unobtainable, slight venous distention present, pulse, 120 per minute. Fluoroscopic showed no definite cardiac pulsation. Operation disclosed no definite cardiac wound, but a hematoma from left internal mammary artery causing tamponade. Recovery was uneventful. Patient was discharged on the eleventh day.

SUMMARY

Reports of successfully treated wounds of the heart are becoming more frequent because of better diagnosis and more aggressive treatment. Death usually occurs from either massive hemorrhage or tamponade. Most of the patients who die before operation succumb

to hemorrhage usually due to gunshot wounds, although in our experience several patients with massive hemorrhage from gunshot wounds have survived following very early operative treatment. Patients with tamponade are much more likely to live long enough for treatment to be instituted and in only 2 of our preoperative deaths was this caused by tamponade. Of the 27 patients in our series who were alive 20 minutes after admission to the accident room, there were 7 deaths. This is a mortality of 25.9 per cent in those cases which presented an opportunity for diagnosis and treatment. That the results improve with experience is shown by the fact that in the last 13 of these cases, there has been but 1 death. Cerebral damage due either to embolism or to anoxemia from neglected tamponade has been the most frequent postoperative complication. No residual

cardiac disability has been observed in patients who recovered. Acute cardiac tamponade may be produced by extracardiac lesions, such as hematomas.

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NONPENETRATING TRAUMA OF THE ABDOMEN

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TRAUMA to the abdominal viscera without laceration or penetration of the abdominal wall or with incomplete penetration presents a particularly fascinating problem and challenge to the surgeon, because of (1) the high mortality attending laceration or rupture of the viscera, (2) the comparative infrequency with which the individual surgeon encounters abdominal trauma, (3) the frequent difficulty in making an accurate diagnosis of a serious lesion because of the apparently inconsequential or obscure initial symptoms, (4) the possibility of a variable latent period before evidence of extensive visceral damage appears, (5) the need for the recognition of the pitfalls in diagnosis and treatment if the extraordinarily high mortality is to be lowered

Injury to the abdomen may result in (1) a simple laceration or puncture of the abdominal wall, which does not perforate into the peritoneum, (2) a penetrating or perforating wound, (3) a contusion or subcutaneous rupture only of the abdominal wall, (4) a contusion, laceration, or rupture of an intra-abdominal organ or structure with no evidence of external injury, (5) any combination of the above four lesions (Levering)

Nonpenetrating trauma of the abdomen will include, then, a contusion or subcutaneous rupture of the abdominal wall, or a contusion, laceration, or rupture of intra-abdominal viscera or blood vessels, either without external injury or with a superficial unrelated nonpenetrating laceration

MORTALITY

Mortality in subcutaneous abdominal visceral trauma is high largely because of the frequency of multiple major injuries which are inevitably and rapidly fatal. However, the reported mortality rate in recent years has shown a definite decrease. This decrease

seems due to improvement in methods of diagnosis and better recognition of the therapeutic indications, especially the appropriate time for surgical interference.

TABLE I — MORTALITY

Author	Years	No. cases	Mortality per cent
Petersen	1885-1890		60-70
Petersen	1900		30
Demel	1933	126	21.9
	to		
Lewis and Trimble	1936	140	20
Just		79	13.9

INCIDENCE

The incidence of subcutaneous trauma of the abdomen as compared to injuries elsewhere in the body is low. In a 5 year period, 2217 injuries of all types were admitted to our clinic only 32 (1.4 per cent) of which had nonpenetrating abdominal trauma. Cody reports similarly 5744 accidental deaths in Iowa during a 3 year period, 53 (0.9 per cent) of which were the result of subcutaneous abdominal trauma. A higher rate of occurrence might be found in densely populated areas where the likelihood of this type of injury as a result of motor accidents would be greater. However, it is obvious that nonpenetrating abdominal trauma is not too frequently encountered except possibly in hospitals devoted largely to traumatic surgery.

ETIOLOGY

Abdominal trauma may result from (1) an anteroposterior or a lateral squeezing, or a direct blow, crushing a viscus between the instrument of force and the spine or rupturing an organ or the diaphragm by a great increase of intra-abdominal pressure, (2) a tangential force, moving the bowel or other viscus beyond its limits of mobility causing tears in mesentery, etc., (3) compression of fluid or gas in a single loop of intestine, (4) fragments of pelvic bones, rupturing or puncturing the bladder and rectum, (5) falls at play, at work, or at home. Motor and indus-

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trial accidents, athletic injuries and falls in the home are the most frequent causes. Of Bailey's 100 cases, 76 were due to transportation accidents (60 motor) the 24 remaining to industrial or athletic accidents, or falls in the home.

PATHOLOGY

In mild cases, usually without evidence of superficial contusion there may be a hematoma deep in the abdominal muscles, secondary to a laceration of a muscle or a blood vessel, a retroperitoneal hematoma, hemorrhage into the mesentery or omentum or beneath the capsule of liver, spleen, or kidney or subserosal hemorrhage of stomach or intestine. It is this group that definitely may be treated conservatively. The frequency with which mild indeterminate trauma is found has been variously reported. In 45 (30 per cent) of 140 cases by Lewis and Trimble, 41 (54 per cent) of 76 cases by Just, and 36 (38 per cent) of 94 cases in our series.

Crushing and severe injuries produce particularly laceration or rupture of the liver, spleen, pancreas, kidney, small or large intestine, stomach, diaphragm, bladder, gall bladder, omentum or mesentery often accompanied by fracture of the pelvis, spine or ribs. Numerous reports of obscure and rarer lesions have also been recorded such as (1) hemoperitoneum due to subcutaneous rupture of the iliac vein (2) mesenteric thrombosis (3) rupture of a gastric ulcer (4) avulsion of the gall bladder (5) pancreatic cyst (6) tuberculous peritonitis, following rupture of an intra-peritoneal tuberculous abscess.

DIAGNOSIS

The successful outcome of most cases hinges upon the sagacity and diagnostic acumen of the attending physician. Clinically abdominal trauma may be classified into three groups (1) severe multiple injuries which are rapidly fatal and for which no treatment is of avail (2) cases that obviously require immediate operation (3) cases in which the diagnosis is doubtful and the indications for or against operation are not clear.

In the proper care of this third group lies the greatest opportunity for saving lives and lowering the extraordinarily high mortality

rate. Very close and repeated observation is mandatory. At the earliest possible interval following the accident a decision must be reached whether or not the lesion demands immediate operation.

Aids toward an accurate diagnosis will be (1) the history (2) careful physical examination (3) blood count, blood protein estimations, urine examinations (4) radiography.

History. It seems generally agreed that force applied to a *limited* or circumscribed area of the abdomen is more prone to lacerate or rupture the intestine or kidney but force applied diffusely over a wide area is likely to injure the liver, spleen, pancreas, bladder or blood vessels. Engorgement or dilatation during physiological activity may predispose to injury. Hence it is important to know the exact character of the blow, the size of the object inflicting the trauma, the details of the accident, the time that has elapsed since the accident, and the previous consumption of food or drink as well as the record of any previous abdominal disease. A detailed and accurate history will aid in estimating the likely extent of the injury.

Examination. The examination of the patient should be thorough and painstaking with consummate weighing of the evidence. The pulse and blood pressure should be noted. A patient with pallor should suggest hemorrhage or primary shock. One of the deceptive features of abdominal trauma is that the primary shock may be transient. Certain cases that are apparently in shock may have a definite elevation of blood pressure. This hypertension has been shown to be due to extensive retroperitoneal hemorrhage or injury particularly about the kidney or adrenal. Retroperitoneal involvement must be suspected, therefore, with hypertension in abdominal trauma. If the patient is in shock a detailed examination must be postponed until treatment for its relief has been effective. However the examination when made, should be complete for injury not only of the abdomen, but of other parts of the body, as multiple injuries are not infrequent.

Abdominal distention, meteorism, localized pain and tenderness, muscle rigidity or spasm, absence or presence of peristalsis and

the type of respiratory excursion must be carefully studied. Early abdominal distention with general abdominal, but not boardlike, rigidity and absence of severe pain, particularly if there is evidence of a concomitant back injury, are indications of injury or irritation of the celiac plexus, and that a conservative policy can be planned. *Increasing* abdominal distention with localized tenderness and rigidity—often boardlike—severe, *persistent*, or recurrent pain, and absence of peristalsis, are indications of a visceral injury, and for immediate operation. Rectal or vaginal examination, particularly when the lesion is in the lower abdomen, may prove of great value. By this procedure, a retroperitoneal rupture of an air-containing viscus may be recognized when palpable emphysema of the pelvis is present.

Either continuous or intermittent pain that is *persistent* and *repeated* vomiting or hematemesis, rising pulse rate, and spreading local tenderness are particularly significant. Vomiting, in itself, is not pathognomonic, but repeated vomiting, or repeated hematemesis and persistent pain may be evidence of visceral injury.

One should not be deceived by a post-traumatic period of comparative comfort or relative normalcy. Years ago (1858), Pollard noted in certain instances of grave abdominal trauma, "the absence of all symptoms *indicating a mortal injury* for upward of two hours." Butler observes that with shock or alcoholism this interval may be lengthened to 6 or 8 hours. Berry has ascribed the *lack* of early significant symptoms in intestinal rupture to the fact that the immediate effect of severe injury to the intestine is a contraction of the bowel in the neighborhood of the lesion which tends for a time to prevent further extravasation of intestinal contents. This contraction may last for many hours. Cases of laceration of the intestine, stomach, bladder, and spleen have been recorded in which the patient has walked and shown no evidence of major casualty only to collapse later.

Blood count and laboratory tests. Immediate, complete blood count and urine examination should be made. Bloody urine indicates kidney, bladder, or urethral injury. If hemor-

rhage is suspected, estimation of the blood specific gravity by the falling-drop method of Barbour and Hamilton can be rapidly made, the concentration of blood plasma protein quickly determined, and prompt information obtained concerning the extent of blood loss. The estimation of blood concentration, if desired, can be checked by hematocrit determination, indications for type and amount of intravenous therapy may thus be obtained.

Radiography. A procedure that is of distinct value in the diagnosis of *intestinal laceration* or rupture is a radiograph of the abdomen. White has suggested that this be taken in the sitting posture so that free gas in the peritoneum can be better recognized by its concentration beneath the diaphragm—a crescent or sickle-shaped gas accumulation over the liver and below the diaphragm. If the patient cannot sit, White advises a lateral x-ray at the level of the diaphragm with the patient prone. Gas beneath the diaphragm when present is positive evidence of intestinal rupture, but *if absent or unrecognized it does not rule out the possibility of intestinal laceration*. Also, gas demonstrable in the retroperitoneal tissues may accompany duodenal rupture.

Intravenous urography and, in carefully selected cases, retrograde cystography and pyelography will be a great aid in the accurate diagnosis of urinary tract lesions, particularly lacerations of bladder and kidney.

Burke and Madigan have suggested the use of thorotrast as an aid in the diagnosis of lacerations of the liver and the spleen. Thorotrast is administered intravenously and an abdominal film is taken 4 hours later.

Peritoneoscopy. Peritoneoscopy may eventually prove of value in the diagnosis of certain obscure lesions but this procedure has not yet been in use sufficiently long to speak with authority concerning its applicability or indications in cases of abdominal trauma. It would seem to be contraindicated where gastrointestinal rupture is suspected. Its field of usefulness is likely to be limited.

Summary. The evidence as elaborated by history, examination, laboratory tests, and x-ray, must be carefully weighed. Abdominal examination is the most important. Severe localized or general persistent abdominal pain,

increasing pulse rate repeated vomiting, localized tenderness and boardlike rigidity with or without evidence of increasing hemorrhage or infection form a combination that demands operative interference.

All cases, no matter how trivial in which a decision for operation cannot be immediately made should be kept under the closest observation and operates withheld. Repeated examinations should be made at least every 30 minutes until a definite conclusion concerning operation can be reached. In an obscure quiescent case illuminating symptoms such as pain distention or rigidity may have a sudden onset. Blood pressure and pulse records should be taken every 15 or 30 minutes. Blood counts should be repeated at short intervals. The repeated blood count may show evidence of hemorrhage by decreasing hemoglobin and red blood count and of advancing infection by an increasing leucocytosis. Decision for or against operation should be made within 4 to 6 hours after the accident. Any delay beyond this period may jeopardize the possibility of saving a life.

As just has stated. In spite of the most painstaking study there will always remain a number of cases in which a definite diagnosis is impossible, but the syndrome is of a type which justifies operation. In these cases an exploratory laparotomy should be done.

SHOCK

Primary shock may be due to (1) extremely painful trauma (2) severe crushing injury and (3) hemorrhage (Butler). Shock is not a necessary accompaniment of every injury; moreover it shows wide variations that may not be at all correlated with the severity of the trauma. Shock should be combatted promptly by application of heat, lowering of the head, elevating of the feet, intravenous infusions of blood plasma, administration of oxygen, and injection of eschatin or adrenal cortical extract, neosynephrin, veritol, or ephedrine. If blood plasma is not available intravenous administration of gum acacia, saline and glucose or whole blood transfusions should be used. Morphine should be withheld until a decision concerning operation has been reached. Im-

mediate operation should not be undertaken until an effort to relieve shock and improve the patient's condition has been made, and a systolic blood pressure of 100 or over is obtained. However patients in shock requiring immediate operation should be treated and observed in accident wards or in or close to operating suites so that as little delay as possible occurs in inaugurating operative procedure as soon as the patient's condition justifies it.

Jakl distinguishes three stages of progression in severe abdominal trauma: (1) shock (2) transient subjective improvement (3) collapse in the case of hemorrhage, or peritonitis in the case of perforation (injury) of a hollow organ.

TREATMENT

Successful treatment to obtain eventual recovery depends upon (1) prompt recognition that intra-abdominal trauma is present (2) prompt decision that an operation is necessary (3) the correct time for and method of operative interference (4) the magnitude of the injury. With multiple extensive injuries early or immediate fatality may be inevitable—the extent of the trauma placing the injured beyond the aid of any treatment.

Treatment may be either conservative or operative.

Conservative treatment is largely symptomatic but may require maintenance of fluid balance and adequate blood concentration by appropriate intravenous therapy and transfusions, especially when vomiting or hemorrhage recurs and particularly in preparation for surgical intervention early or late. In rupture of the hollow viscera, either actual or suspected particularly of the intestine or bladder some form of sulfonamide therapy is definitely indicated—sodium sulfathiazole intravenously or sulfanilamide by hypodermoclysis is preferable, as it is not likely that these drugs will be readily tolerated by oral administration. Lesions of the hollow viscera will demand early operation but solid visceral injuries, unless accompanied by persistent and unrestricted hemorrhage may more properly be considered candidates for temporary conservative measures and for delayed or late operation.

Operation may be indicated either early or late. Early operation should take place within 6 hours of the accident, particularly when injury to hollow viscera seems likely. Late operation will be demanded by evidence of progressive or recurrent hemorrhage, extensive visceral damage or local tumor formation indicating unresolved hematomas, local abscesses, or actual neoplasm (pancreatic cyst, etc.)

The common intra-abdominal lesions are lacerations or rupture of the liver, spleen, kidney, intestine, and bladder. Their specific treatment will be briefly outlined.

Liver When the patient is not moribund and when there is definite evidence of unchecked hemorrhage, operation is indicated. Without evidence of severe and persistent hemorrhage conservative treatment should suffice though with late recurrent hemorrhage operation may be required. Transfusion or blood plasma may be necessary before, during, and after operation. On exploration, if there is still bleeding from the liver this may be arrested by digital compression of the hepatic artery and portal vein at the foramen of Winslow and the laceration may be sutured or the hemorrhage controlled by tamponade and suture. Drainage should be instituted to facilitate the extra-abdominal escape of bile leaking from the laceration. If, on exploration, the hemorrhage seems controlled or has ceased it has been suggested that blood in the peritoneal cavity may be gently evacuated by suction, but clots in the rent in the liver had best not be disturbed as fatal and uncontrollable hemorrhage has occurred from overzealous efforts to suture a laceration when hemorrhage has ceased. Suture in this case is not necessary as spontaneous healing can take place. Trimble has pointed out the danger of reinfusion or transfusion of the blood taken from the peritoneal cavity in rupture of the liver. Toxic symptoms may follow, several fatal results have been recorded. Mortality rate from liver rupture is approximately 50 per cent due largely to the inefficacy of any treatment in extensive laceration.

Spleen If the patient's blood pressure is low or he is in shock—blood plasma or a transfusion should be administered. Opera-

tion should take place as soon as the blood pressure is over 100, and transfusion should be continued during and following the operative procedure. The intraperitoneal blood may be ladled or aspirated out into a sterile flask, citrated and reinfused into a vein. This may often prove a life-saving measure. Spinal anesthesia has much to recommend it. Splenectomy is to be preferred to suture or tamponade of the laceration. The mortality rate is 30 per cent largely because of associated extensive trauma.

Kidney Most of the injuries to the kidney are contusions, which heal spontaneously, and expectant treatment will suffice. However, in the remainder in which the capsule or the pelvis is torn, operation will be necessary and, if deferred too long, may not save the patient. Reported statistics indicate that 20 to 30 per cent will require surgery (Just, Lewis and Trimble, Prather, Peacock). The indications for operation are gross infection, persistent hematuria, evidence of urinary extravasation, and loss of renal function. Intravenous urography will help determine the extent of damage to the kidney and in doubtful cases may confirm the necessity for operation. Retrograde pyelography should be resorted to with extreme caution and only when indications for operation cannot be determined by other means. Peacock observed a fatal secondary hemorrhage following this procedure.

Suture of the kidney will usually suffice, but nephrectomy will at times be necessary. The recorded mortality varies from 16 to 30 per cent depending upon the frequency of multiple associated lesions and upon delay in operation in those cases requiring surgery.

Intestine Early operation after treatment of any initial shock is imperative in intestinal rupture and preferably should take place within 6 hours of the accident. Mortality mounts rapidly with delay beyond that period. Therefore, close and frequent observation and re-examination of doubtful or suspicious cases during *this interval particularly* are obligatory.

Spinal anesthesia facilitates the operative procedure which should be carried out as gently and as rapidly as possible. Suture of the laceration is usually sufficient, this is best done transversely rather than longi-

tudinally (to the long axis of the bowel). With multiple lacerations or extensive mesenteric laceration resection may be necessary. In desperate cases and particularly in large intestinal rupture, obstructive resection, exteriorization, or colostomy may be advisable. Sulfanilamide or sulfathiazole may be used locally in the peritoneum and routinely parenterally as part of the postoperative therapy.

The reported mortality is extraordinarily high. Most recent statistics cite a 60 to 10 per cent rate (Petry, Beitler, Lewis, Estes, Just). Of 1476 cases recently collected by Poer from the literature, the total mortality was 72.1 per cent and the postoperative mortality in 1914 was 59.5 per cent. This may be ascribed to peritonitis, delayed operation, large and multiple lacerations, extensive hemorrhage and to associated injuries, particularly laceration of the mesentery. Early diagnosis and early operation should tend to lower what would seem to be an unnecessarily high mortality.

Bladder. In rupture of the bladder suture of the rent in its wall, control of hemorrhage and drainage of the area of extravasated urine will be necessary. The rupture may be intra-peritoneal or extraperitoneal and diagnosis will be facilitated by either intravenous urography or retrograde cystography. Fracture of the pelvis is frequently a concomitant lesion. Care of the bladder tear will not interfere with its appropriate treatment. Postoperative sulfanilamide or sulfathiazole therapy will be advisable. The reported mortality ranges from 14.4 per cent (Peacock) to 6.25 per cent (Culver and Baker). It results from other associated severe injuries, massive hemorrhage from laceration of large pelvic blood vessels and delay in operation (peritonitis). Early recognition of rupture and early operation are imperative.

CONCLUSION

Nonpenetrating trauma to the abdomen may result in an injury that may be treated either by conservative means or operative interference.

Successful treatment depends upon (1) prompt recognition that an intra-abdominal

lesion is present (2) prompt decision that an operation is necessary (3) the correct time for and method of operation (4) the magnitude of the injury.

Clinically the cases may be classified into three groups: (1) Severe multiple injuries which are rapidly fatal and for which no treatment is of avail (2) cases that obviously require immediate operation (3) cases in which the diagnosis is doubtful and the indications for or against operation are not clear.

The history, careful physical examination, repeated blood counts, blood specific gravity and blood protein determinations, urine examination, and roentgenography of the abdomen should be helpful in establishing the diagnosis. In doubtful cases only by frequent repeated re-examination (30 minute intervals) will the developing evidence of a serious lesion be recognized in time to suggest operation before it is too late. Every case of abdominal trauma, therefore, no matter how apparently slight, should be kept under close observation until a sufficient interval has elapsed to determine whether an operation is indicated or not, or until recovery is assured. Lesions of the hollow viscera will demand early operation. Solid visceral injuries, unless accompanied by persistent and unrestricted hemorrhage may more properly be considered candidates for delayed or late operation. Only by close constant supervision and the prompt recognition of an intra-abdominal catastrophe demanding operation can the extraordinarily high mortality in abdominal injury be lowered.

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GUNSHOT WOUNDS OF THE ABDOMEN

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THE general category of gunshot wounds of the abdomen now includes not only injuries due to bullets fired from rifles, revolvers, or machine guns, but those wounds peculiar to warfare which are caused by fragments of shells, bombs, and hand grenades, as well as the "blast" injuries produced by detonation of high explosives

The problems involved in the management of abdominal war wounds, as well as the seriousness of such injuries, are summarized in the report of the Medical Department of the United States Army in the World War as follows "The man with an abdominal wound presents one of the serious problems which the military surgeon has to face. No other group of cases furnishes anything comparable to it in testing the medical resources of an army, or the technical skill of its surgeons"

This review will be limited to a consideration of the modifications of procedure and the recent advances in surgical practice which, in some measure, offset the grave consequences of abdominal wounds due to gunfire

Collection, transportation, and facilities for early treatment Improved highways, motor ambulance transportation, and even transfer of casualty cases by airplane, have greatly facilitated the rapid removal of patients to hospitals. The importance of providing an adequate supply of oxygen and of preventing extravasation of intestinal contents due to reduced atmospheric pressure at high altitudes has been discussed by Lovelace, who advocates the use of heated sealed pressure cabin airplanes, equipped with apparatus for the administration of oxygen

The development of mobile military surgical units has made operative treatment possible within 6, or at most 12, hours after injury has been incurred, thus reducing the number

of hopelessly delayed cases. In civil practice, the same improvements in transportation and the greater number of well equipped hospitals in small communities likewise permit more adequate and prompt treatment

Methods for reducing the incidence and seriousness of wounds due to gunfire The value of body armor as a means of deflecting bullets or of arresting projectiles which are travelling at such a low velocity that they would ordinarily be retained is manifest. The arguments which have been advanced for and against this method of protection, as well as a detailed discussion of various materials and designs for armor, are included in a previous report by Storck. The demonstration by Zuckerman that body ensheathment is protective against "blast" injuries coupled with the fact that body armor has been successfully used in the present European war establish the value of this preventive measure

The possibility of reducing the severity of peritonitis caused by penetrating wounds of the abdomen through alteration of the intestinal flora by replacement with nonpathogenic bacteria, or by sterilization of the bowel contents through administration of intestinal antiseptics, has been considered in a previous communication by the present author (12). The efficacy of tetanus toxoid immunization has been proved and this simple expedient may be depended upon to avert the deaths which occur among patients with abdominal gunshot wounds who would have survived the visceral lesions alone

Improved methods of study and estimation of the status of patients with known or suspected abdominal injuries The duration and degree of shock and hemorrhage often determine the outcome in patients with gunshot wounds of the abdomen, and these factors are of paramount importance both in the selection of cases requiring operative intervention and in the timing of operation. Earlier detection of the existence and progress of shock and hemorrhage is now possible by combining the meth-

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ods presently available for revealing changes in blood concentration with the older methods for the study of these conditions. Determination of blood specific gravity by means of the falling drop apparatus and estimation of mean corpuscular volume are simple and quick procedures which permit prompt recognition of the presence of or fluctuations in the degree of shock and hemorrhage.

Peritoneoscopy although inadequate for determining definitely whether or not visceral perforation has occurred may avert unnecessary laparotomy or on the other hand may indicate a need for abdominal exploration not revealed by other methods of examination. If proper technical precautions are observed the finding of hemoperitoneum is evidence of penetration of the abdominal wall.

Intravenous pyeloureterography and retrograde cystography make possible more accurate visualization of presence or extent of injuries to kidneys, ureters and bladder.

Treatment of shock and hemorrhage. The evolution of methods for preserving and administering whole blood and liquid or dried plasma along with the development of more accurate means of determining the degree and progress of shock and hemorrhage have in no type of surgical cases been of greater benefit than to patients with gunshot wounds of the abdomen. There are prospects that the supplies of blood elements available for use in emergencies will be further augmented through the isolation of bovine serum albumen suitable for treatment of shock and hemorrhage in the human.

Observations reported by Kekwick, Marriott, Maycock, and Whitby indicate that plasma and whole blood are equally effective for restoring blood volume, and that with large transfusions only 1 pint in each 3 pints of plasma and blood administered need be whole blood. As a rule in secondary shock, a rise of from 10 to 20 millimeters of mercury can be anticipated from every 540 cubic centimeters of blood transfused, provided that bleeding has ceased and that no other causes of loss of circulatory fluid are operating. Differentiation is to be made between primary shock due to psychogenic and neurogenic influences from which recovery rapidly occurs following rest

and the administration of morphine and secondary shock, which is indicated by a persistence of systolic blood pressure below 100 millimeters of mercury even after 1 hour of treatment by simple measures, and in which transfusion is necessary. Practically complete replacement of lost fluid is required, and at least half of this should be protein fluid, as otherwise the restoration of blood pressure will be only temporary. Transfusions of as much as 3,000 cubic centimeters within a few hours following injury may be required to afford the full benefit attainable by this type of therapy.

The demonstration by Schnedorf and Orr of the value of oxygen therapy in controlling shock has added to the presently available methods for treating this frequent concomitant condition of gunshot wounds of the abdomen. The evidences advanced by Scudder, Bemer and others of the efficacy of adrenal cortex extract, as well as the observations of Best and Solandt concerning the beneficial effects of pituitary extract and concentrated serum in combatting shock, indicate that these forms of therapy are of definite value.

The thrombin preparation, which Smith and his co-workers have found to be so effective in arresting hemorrhage when topically applied, meets the need for the control of bleeding from liver lacerations when hemostasis by other means is difficult or impossible.

Management of ileus and peritonitis. By the very nature of the wounds and the operative manipulation necessary for their repair, gunshot injuries of the abdomen are inevitably accompanied by some degree of ileus and usually by more or less diffuse peritonitis.

Attempts to remove contaminating material from the peritoneal cavity by lavage are not only futile but actually increase the extent of infection and add to already existing shock. The impossibility of effectively draining the peritoneal cavity even by the introduction of multiple drains and the danger of intestinal obstruction due to the presence of drains are now generally recognized. The notoriously poor results obtained by performing enterostomy for the purpose of preventing or relieving ileus are in sharp contrast to the usually satisfactory control of this condition by doses of

morphine sufficient to maintain intestinal tone and by the use of the Miller-Abbott tube, in conjunction, if necessary, with the administration of oxygen for the removal of nitrogen from the intestine, as suggested by Fine, Banks, and Hermanson. The report by Fine, Hurwitz, and Mark concerning the serum content of the fluid present in the lumen of distended loops of bowel and the resulting depletion of plasma proteins in the circulating blood emphasizes the importance of plasma transfusion as a rational part of the therapy of ileus. Degeneration of the adrenal cortex as a result of both ileus and peritonitis occurs so constantly as to imply the need for the administration of adrenal cortical hormone or desoxycorticosterone acetate in the treatment of either or both of these conditions.

Evidences of the efficacy of sulfonamide drugs, both introduced directly into the peritoneal cavity and given parenterally, in preventing or reducing the severity of peritonitis are so numerous and convincing as to leave little doubt that these drugs should be used when peritoneal contamination has occurred.

Penicillin, the bacteriostatic fungus extract which has been the subject of a report by Florey and his associates, and gramicidin, an antibacterial substance obtained from sporulating bacilli and described by Dubos and Hotchkiss, are not rendered ineffective by the para-aminobenzoic acid present in inflammatory processes, and give promise of being useful in the treatment of infections which do not respond to the sulfonamide drugs.

Prevention and treatment of wound infection and wound rupture. The morbidity and mortality in gunshot wounds of the abdomen, due to wound rupture, are lessened by supplementing épluchage and closure of wounds by means of nonabsorbable suture materials, with maintenance of normal plasma protein levels and the prevention of avitaminosis. These same measures, particularly when combined with the instillation into contaminated wounds of sulfonamide drugs, zinc peroxide paste, or other oxidizing antiseptics, or with the delayed closure and adequate drainage of such wounds, greatly reduce the incidence of serious wound infections.

Methods for the prevention and treatment of complications. Through the parenteral administration of glucose and lactated Ringer's solutions, blood plasma, amino-acids, and vitamins, serious nutritional deficiencies can be prevented for at least several weeks.

Fatalities due to pulmonary complications can be maintained at a minimum by early mobilization and deep breathing exercises or tracheal aspiration for the prevention of atelectasis, and by prompt treatment of pneumonitis with specific antisera and sulfonamide drugs. The high mortality in gunshot wounds of the abdomen when associated with "sucking" or "blowing" chest wounds can be lessened by immediate relief of tension pneumothorax and by the closure of thoracic wounds either by approximation of wound edges or the application of airtight dressings which prevent paradoxical respiration.

Recognition of the frequency with which subphrenic, subhepatic, cul-de-sac, iliac fossa, perirenal, and miscellaneous other residual abscesses occur, and adequate drainage following their early detection by means of x-ray or physical examination, avert the deaths due to these complications. Retained shell fragments or other foreign bodies present in such areas of suppuration should, as a rule, be removed at the time that drainage is established.

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TREATMENT OF BURNS

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THE problems associated with the treatment of the severely burned patient continue to interest the clinician and the laboratory worker. A review of the literature (14) on burns published during the past 15 years indicates changing ideas and intelligent thinking regarding therapy. A few of the older principles of treatment have been continually emphasized, but as our knowledge of physiology and pathology in relation to the changes occurring in the human body increases, recent advances have been made which develop a more rational basis for therapy (18). The interchange of ideas and experiences, together with the emphasis of certain important points, have developed a better understanding of the problem. There can be no outline of treatment for general use as each burned patient deserves individual consideration. A résumé of our present form of management of the severe burn is presented together with a discussion of some of the many ideas advanced relative to present day treatment.

Prior to the publication of Davidson's work (10) in 1925 relative to the use of tannic acid it was the practice of the individual clinician as well as the various clinics and hospitals, to adhere to a routine founded on the experiences of either the surgeon or the clinic. The results obtained in many instances were assumed to be satisfactory. The statistical studies, however, showed that the results were far from gratifying. The morbidity was prolonged and the mortality was high, varying from 30 to 40 per cent (Table I).

Wells has stated "the introduction of tannic acid by Davidson has revolutionized and, apparently for the first time in history standardized the treatment of diffuse burns." The use of tannic acid in the treatment of thermal

injuries has maintained a well deserved place in the regimen of many surgeons. It is entirely in keeping with general progress in medical science that many changes have developed regarding therapy. However the basic concept of toxic absorption from the site of a severe burn which led to Davidson's work, although challenged by many, has not in our opinion been satisfactorily disproved. Like wise in many instances, criticism of the tannic acid method of treatment is unjustified due to the failure of the critics to recognize the basic surgical principles underlying this form of therapy.

FACTORS INFLUENCING THE PROGNOSIS

A combination of factors influences the prognosis for recovery in the case of every severely burned patient. The general care of the patient is of primary importance. Emphasis in recent years has been placed on the therapeutic measures of value in combating the effects of disturbances in general tissue metabolism. It is important to recognize shock and to treat this condition adequately before consideration is given to the local lesion. The extent of the burn bears some relation to the severity of shock but is not to be relied upon inasmuch as this reaction may accompany burns of a lesser degree. Shock should be treated by the application of heat, the administration of sedatives, and the usual supportive measures. Blood plasma is of definite benefit in the treatment of shock accompanying severe burns (17). Intravenous saline and glucose solutions are essential to prevent anhydremia in second and third degree burns. Hemoconcentration is present early in the case of severe burns, with the red blood cell count, blood nitrogen, and blood sugar elevated while the blood chlorides are reduced. It is doubtful if hyperglycemia can be explained as due to hemoconcentration, although dehydration will produce an increase in sugar by accelerating glycogenolysis. A

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lowered serum protein appearing after a few days indicates the need for a blood transfusion or plasma. Whole blood should also be given later in the course of treatment, if secondary anemia develops.

In the case of the severely burned patient, there is a rapid increase in the hematocrit reading during the first 6 hours. During the following 12 hours there is a gradual increase with very little change later. A study of the blood of a patient with an extensive burn showed that the hematocrit was 71 per cent at the end of the first hour (23), a fact indicating that there has been a loss of approximately half of the plasma volume. It was found that giving the adult 5,000 to 6,000 cubic centimeters of saline solution intravenously during a 24 hour period caused a marked drop in plasma proteins, frequently to the edema level. Similar observations have been reported by others (15, 17). Therefore, it is advisable to utilize glucose solution to combat dehydration, and to limit the use of saline. Intravenous blood plasma decreases the hemoconcentration more effectively, without causing a drop in the plasma proteins. Whole blood given with moderate amounts of saline will tend to prevent a marked drop in plasma proteins, but does not reduce the hematocrit as rapidly as plasma. Burns involving a third or more of the body in the adult are now given 1,000 cubic centimeters of blood plasma and 1,000 to 2,000 cubic centimeters of glucose and saline solutions intravenously in a 24 hour period. The remaining amount of required fluid is given orally.

Saline and glucose solutions temporarily raise the blood pressure and may be given to fortify the patient until blood is available. The temporary action of these agents is due to their rapid elimination by the kidneys, blood on the other hand is retained longer because of its protein content. Of the blood, the serum alone is vital to this action (9). Hospitals with blood banks have serum or plasma available for immediate use.

Underhill, Kapsnow, and Fisk maintain that following a burn, the permeability of the capillaries is in one direction only, namely, from the capillaries to the tissues. If only saline or glucose solutions are available, the

TABLE I — COMPARATIVE MORTALITY WITH TANNIC ACID AND OTHER METHODS¹

Author	Other methods		Tannic acid	
	No of patients	Mortality per cent	No of patients	Mortality per cent
Bancroft and Rogers (New York)	90	40.0	114	20.0
Beckman (New York)	320	37.8	114	14.9
Wilson (Edinburgh)	300	38.7	117	11.1
Harris (Toronto)		26.6		12.0
Mason (Philadelphia)	91	28.5	87	13.3
Langer (Vienna)	86	16.3	65	7.7
Mitchner (London)	243	0.4	249	2.4
McClure and Allen (Detroit)	118	9.3	358	11.7
Glover (Cleveland)	121	14.0	809	8.4
Total patients	1369		1013	
Average mortality		24.5		11.3

¹From DONALD M. GLOVER and ARNOLD F. SYDOW. *Am. J. Surg.* 1941, 51: 601.

administration of adrenal cortex hormone may be of added benefit, as it is claimed to restore and maintain capillary tone. The clinical experiences of Wilson, Rowley, and Gray (26) show favorable results as regards the use of an extract of suprarenal cortex. Satisfactory responses have also been reported with the use of the synthetic analogue desoxycorticosterone acetate (27). Rhoads, Wolff, and Lec conclude from their observations that adrenal cortical extract is of value in the treatment of the fluid shift occurring in patients after severe burns and reduces the amount of plasma which is required to restore the circulation to normal.

There has been some question regarding the changes in blood potassium in the production of the toxic symptoms associated with severe burns. The work of Tenery showed that the whole blood potassium varied directly with the hematocrit changes and the plasma potassium findings were not important. The plasma potassium levels are usually increased during the first 48 hours. In the patients studied the potassium did not reach a toxic level. Toxic symptoms of burns were present without the presence of a toxic potassium level. Scudder found in a study of plasma potassium in 6 cases with severe burns an elevation similar to those he found in other forms of shock.

TABLE II.—REPORTED CAUSES OF BURNS TAKEN FROM THE HOSPITAL RECORDS 1922-1940¹

Cases	No. of cases	Percent
Hot fluids (spilling hot liquids from table or stove stepping or falling in hot water)	563	55.3
Fire (bonfire stove gas heater gasoline etc.)	263	5.8
Fire (result of playing with matches)	63	6.7
Chemicals	40	3.9
Not stated	24	2.3
Total	1000	
Considered avoidable	830	80.5
Considered unavoidable	14	1.3
Not stated	24	2.3
Total	868	

¹From the Children's Hospital of Michigan

SURGICAL MANAGEMENT

An extensive burn lesion may be compared to a large open wound and deserves rigid aseptic surgical care. The importance of thorough cleansing combined with débridement of the involved skin areas, cannot be too strongly emphasized. This includes the removal of all foreign material and necrotic tissue, the opening of blebs and blisters, and the removal of loose skin, together with gentle but complete cleansing of the involved surfaces with saline and boric acid solutions. The use of green soap and solvents, such as ether and alcohol may be necessary. The burn resulting from acid or an alkali should always be thoroughly washed with water before the neutralizing agent is applied (11). Sodium bicarbonate solution is effective in acid burns, and acetic acid may be used as the neutralizing agent in burns from alkalis. In most instances the proper preparation of the burned area may be successfully carried out with little pain by the use of sedatives, such as codeine in the case of young children and morphine in older individuals. Light anesthesia may be required if the procedure necessary to prepare the involved area causes severe pain. Sodium pentathal administered intravenously by a competent anesthetist provides a satisfactory type of anesthesia for the preparation of extensive burned surfaces. (Table II.)

Failure to adhere to the basic surgical procedures in the preparation of the burned area, either because of lack of familiarity with their importance or because of existing conditions

as met with in war zones, has led to adverse criticism of the tannic acid method used in the treatment of the diffuse burns seen in civil life. In peacetime casualties are usually hospitalized within a short time, but under war conditions many days may elapse before the patient is given proper care (12). This in our opinion has been the chief factor accounting for the disappointing results of the tannic acid treatment of burns in modern warfare.

TOXEMIA OF BURNS

The factors involved in the development of the toxemia which accompanies severe and extensive burns have been widely discussed. Uniformity of opinion on this question is lacking. That infection may be responsible in many cases seems probable. On the basis of bacterial invasion of the local lesion together with the presence of concurrent infections in many young patients, we instituted chemotherapy in 1939 (18). In our first patients sulfapyridine was given orally and when sulfathiazole became available, this drug was substituted because of claims of decreased toxicity. In the absence of any accepted contraindications, chemotherapy is instituted when the temperature reaches 103 degrees F. The dosage in the case of children is calculated on the basis of weight. A total of 13½ grains per pound of weight is given in the 24 hour period in divided doses at 4 or 5 hour intervals. In the case of adults 1 gram is given every 4 hours. The dosage is then governed by frequent blood level determinations. A level near 4 milligrams per 100 cubic centimeters is desirable. Close clinical observations for complications or unfavorable reactions are necessary, and frequent blood and urine studies are advisable. A favorable clinical response with a decline in temperature is usually apparent in a few hours. There has been no deaths or serious reactions in approximately 75 severely burned patients treated to date by the addition of chemotherapy.

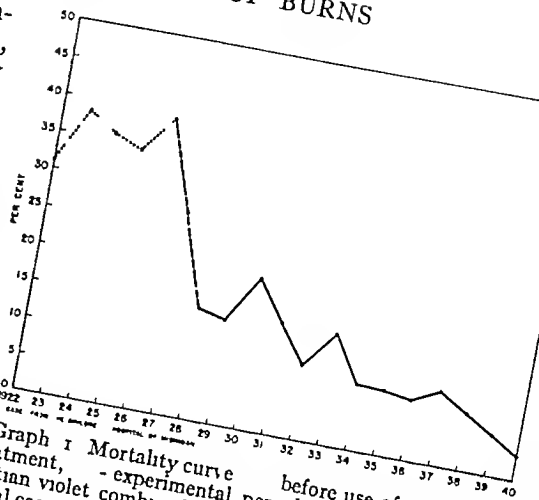
LOCAL USE OF SULFONAMIDE DERIVATIVES

In recent months the suggested use of certain sulfonamide derivatives as a local treatment for cutaneous burns has been proposed. This form of therapy may aid in the preven-

tion of local infection or retard bacterial invasion. Also, since the drug is absorbed, beneficial effects in the case of septicemia may be apparent. Our experience with this form of therapy is limited to an experimental study of a small group of patients treated locally with the sodium salt of sulfathiazole in a water soluble ointment base. Several patients with burns approximating 20 per cent of the total body surface have been treated and responded favorably with the formation of a dry crust, which remained intact and allowed healing without evidence of infection. We believe, however, that this form of therapy is not without certain danger. The rate of absorption is not controlled and high blood levels may occur, particularly in patients with a diminished urinary output. The formation of the kidneys and in the pelvis of the cause serious symptoms due to obstruction. This occurred in one case in our series. Basing an opinion on our limited experience, we believe further experimental study is indicated, together with wider clinical use before local application of the sulfonamide derivatives can be generally recommended. Pickrell has recently advocated spraying cutaneous burns with a 3 per cent solution of sulfadiazine in 8 per cent triethanolamine with satisfactory results in over one hundred cases.

TANNIC ACID

The details of the tannic acid treatment have been outlined in previously published papers (4, 13, 14, 16, 18, 22), but certain important features of this form of therapy deserve repetition. The use of the freshly prepared aqueous solution of tannic acid in 5 per cent strength as a coagulant of the protein on the surface of a burned area has stood the test of time. The application by spraying has been successful and is still popular. Prepared tannic acid strength may be substituted when the freshly prepared solution is not available. The technique proposed by Bettman (5, 6) combines the use of a solution of 10 per cent silver nitrate and a 5 per cent tannic acid solution. The tannic acid is applied either as a spray or in jelly form, followed shortly by the



Graph 1 Mortality curve
treatment, - experimental period, — tannic acid and
gentian violet combined with silver nitrate (10 per cent)
Total cases 1,018

application of the silver nitrate solution. The claims for this technique, as stated by Bettman, have been substantiated, and we believe that this adjunct to the original tannic acid treatment has proved of distinct value.

GENTIAN VIOLET

Gentian violet in a 1 per cent aqueous solution as advocated by Aldrich (1) is preferred in burns showing evidence of infection when first seen, or in cases of more than forty-eight hours' duration when first treated. Burns involving the perineum, the hands and feet, and deep burns encircling the extremities or in the region of joints should be treated with gentian violet solution. The coagulum produced by gentian violet is more pliable and obviates splitting of the protective coating over joint areas and permits increased freedom of the hands and feet. The dye may also be combined in the treatment, after the use of tannic acid, when there is separation and evidence of infection about the edges of the coagulum.

GENTIAN VIOLET AND SILVER NITRATE

Following the experience with silver nitrate combined with tannic acid, a similar technique was used, gentian violet being substituted for tannic acid. The results in a small series of cases were satisfactory and provided the basis for a published report (8). This combination has to some extent offset certain disadvantages of the gentian violet solution when used

alone. A firmer coagulum is produced drying is more rapid and the disagreeable staining properties are somewhat limited. In addition, the antiseptic properties of the gentian violet solution appear to be increased by the combination with silver nitrate. Aldrich (2) at present advocates the use of a triple dye preparation namely crystal violet, brilliant green, and neutral acriflavine for the purpose of a more complete antiseptic action. We have had no experience with this combination.

BURNS OF HANDS AND FACE

Allen has re-emphasized and called attention to the value of aseptic surgical preparation of burns of the hand. Following thorough cleansing of the burned area, the entire surface is covered with a nonadherent type of dressing such as petrolatum gauze. A voluminous soft dressing is then applied and bandaged to exert pressure to all parts involved thus minimizing edema and the loss of tissue fluid. The part is then splinted in the position of function. Fourteen days later the original dressing is removed and the less seriously burned areas are usually found healed. Burns of the face deserve special consideration and should not be treated by any stereotype method. Tannic acid jelly may be used effectively for certain burns of this type but in other instances it may be of advantage to apply saline compresses or Blair's jelly (7) together with the application of pressure.

LATER TREATMENT

The details of the treatment following the separation of the tannic acid or gentian violet coagulum have been previously published (18). However emphasis should again be placed on the value of early skin grafting. Early grafting of extensive granulating surfaces has saved many lives and should be resorted to as soon as the local lesion is sufficiently prepared to assure successful results. This practice has also aided in minimizing scarring and deformity in many instances. (Graph 1)

CONCLUSIONS

1. It is important that careful attention be given to the treatment of shock accompanying the diffuse burn.

2. Surgical preparation of the burned area should be performed with the most rigid aseptic technique.

3. The choice of local treatment depends on the location of the burn and the time that has elapsed before therapy is instituted.

4. The maintenance of the fluid and the electrolytic balance as well as attention to the nutrition of the patient is essential.

5. Measures must be taken to combat infection with the addition of chemotherapy.

6. Early skin grafting minimizes the loss of fluid from the burned area, prevents the development of chronic infection, and aids in limiting scarring and contractures.

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SOME PROBLEMS CONCERNING ACTIVE IMMUNIZATION AGAINST TETANUS

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THE present war and the consequent mobilization of millions of soldiers throughout the world have given a great impetus to the use of toxoid in active immunization against tetanus. Formerly the medical profession in general, with the notable exception of the French, had been rather indifferent to its possibilities. Protection against tetanus, however, is not only a necessary measure in time of war. Infrequent as it is in peace, tetanus is still common enough to be a matter of grave concern, especially in view of the fact that the mortality, though reduced somewhat in recent years by a better understanding of the pathogenesis and treatment of the disease, is still alarmingly high.

Although prophylactic passive immunization with antitoxin has proved very helpful, no one will deny that it leaves much to be desired. One is interminably confronted with the question whether antitoxin should be given in a particular instance. No means of properly determining this issue is available. Anyone who has been called upon to treat tetanus which has resulted from some trivial and apparently clean laceration or abrasion will know forever that it is not only deep contused and punctured wounds incurred in the street or the barnyard that may harbor actively growing *Clostridium tetani*. Tetanus not infrequently has followed an injury so inconspicuous that no doctor has been consulted, indeed, cases are sometimes seen in which no portal of entry can be demonstrated and in which, naturally, no prophylactic antitoxin has been given. Passive immunization is imperfect also because of the transient character of the protection afforded. The fall in

titer after the first week or 10 days necessitates reimmunization after this interval in all cases of persistent infection and in all of those in which manipulation or exploration must be carried out again. Even such precautions must be in those cases of latent toxemia in which the organisms have been growing unobtrusively in apparently clean and healing wounds. The usual dose may be insufficient in case of overwhelming infection. Finally, there is the question of sensitivity, a matter of great concern both in hazard to the patient and in disability and loss of time from work. It is all the more a problem because of the fact that large groups of persons requiring treatment for injuries are notoriously apt to incur other injuries necessitating subsequent injections of antitoxin, for example, industrial workers and children. In addition, there are the matters of expense and difficulty of storage and transportation. Furthermore, the modern method of warfare with its extreme mobility and lack of any fixed line of battle renders the prompt administration of antitoxin to all wounded a matter of almost unsurmountable difficulty. Obviously a more permanent active immunity which can be brought about prior to the time of injury and by a method relatively free of reactions offers many advantages.

A great deal has been learned about tetanus toxoid and the immunity it confers since Ramon and his associates demonstrated that toxin could be completely detoxified and still retain its antigenic properties and that it could be applied to clinical use (7, 34).

Two types of toxoid are available, plain and alum-precipitated toxoid. When the antigenicity of the two has been compared by individual workers the alum-precipitated toxoid has been found to produce a better antitoxin response (9, 15, 18, 29). Nevertheless, techniques have been worked out with

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children had 0.01 unit, 14 per cent 0.1 unit and 22 per cent 0.25 unit, only 2 children having less than 0.01 unit. Whether McBryde's finding of larger amounts of antitoxin in children is linked with the proportionately larger amount of toxoid per unit of body weight which they received as compared with adults on whom most of these studies have been made, is a matter to be considered.

There is no simple method of testing immunity against tetanus in man, the only method at our disposal being the bio-assay in laboratory animals of the blood serum for antitoxin. One would like to know what titer level is necessary for adequate protection. Ramon (26) was of the opinion that 0.001 international unit represented a protective level in man because horses, which he feels are of the same order of sensitivity, survive the introduction of a splinter infected with a lethal dose of spores when their serum contains this amount of antitoxin. Sneath, Kerslake, and Scruby (29) suggested that 0.01 unit per cubic centimeter is the protective level in man since this titer in guinea pigs affords protection against a lethal spore dose. Cowles concluded from antitoxin titers in man following injection of 1,500 units of antitoxin, and in guinea pigs and mice at the time of infection with spores, that 0.1 or 0.2 unit can give a fairly certain protection. Gold (12) was of the opinion that we should aim at 0.1 unit or more in active immunization because of his antitoxin estimations in subjects given 1,500 units of antitoxin. Since it is impossible to be certain what antitoxin titer constitutes a protective level, it is also impossible to state with certainty how long immunity lasts after a basic course of immunization. Numerous authors have shown appreciable amounts of antitoxin to be present months or years after a course of immunization. Gold (10) found 0.1 unit or more in 92 per cent of subjects 3 months after two injections of alum-precipitated toxoid, 71 per cent in 6 months, 56 per cent in 1 year, 30 per cent in 2 years.

The question has indeed been raised whether antitoxin titer *per se* is in reality a true index of the degree of immunity. Numerous authors have confirmed Ramon's observation that im-

TABLE II—EFFECT OF A SINGLE NONFATAL DOSE OF TOXIN ON THE ANTITOXIN TITER OF GUINEA PIGS WHICH HAD BEEN GIVEN A SINGLE INJECTION OF TOXOID ONE MONTH PREVIOUSLY*

Amount toxoid in c.c.	Toxin given 1 month after toxoid	Antitoxin titer in American units per c.c. of serum at intervals after injection of toxoid		
		3 months	4 months	6 months
1.0	No	3.0 3.0 4.0+ >4.0 >4.0	1.0 1.0 1.0-2.0 1.0-2.0 2.0 2.0+	
	Yes	>4.0 >4.0 >4.0 >10.0		5.0-10.0 10.0-15.0 >15.0
0.1	No		0.5 0.1-0.5 0.1-0.5 0.1-0.5 0.1-0.5 >0.5 >0.5	
	Yes	>1.0 >1.0 >1.0		>10.0 10.0-20.0 20.0-50.0
0.01	No	<0.01 <0.01 <0.01 <0.01 0.01 0.05+ >0.05		<0.05
	Yes	>0.05		>0.1 >0.1

*The amounts of toxin administered varied as can be seen in Table III.

munized subjects will respond to a subsequent injection with a prompt rise in antitoxin titer. Analyzing reported blood serum titrations on 300 individuals after such "repeat" injections, I find that in 1 week all had 0.01 unit or more, all save 9 had 0.1 unit or more, 204 had 0.5 unit or more. There is no doubt that this capacity of the actively immunized subject to respond quickly to a repeat dose of toxoid is a most important consideration in the efficacy of toxoid as an immunizing agent.

It is important to know whether the toxin produced in the course of the natural disease will similarly serve to cause a prompt elevation of the antitoxin titer in immunized subjects. It has been known for some time that large doses of toxin are antigenic in horses, and toxin is used in conjunction with toxoid in the hyperimmunization of horses for the production of commercial antitoxin. Table II illustrates the fact that toxin brings about a decided increase in the titer of immunized guinea pigs. Three months after 1.0 cubic centimeter of toxoid has been given to guinea pigs and 2 months after varying doses of

TABLE III.—RELATIONSHIP BETWEEN SERUM ANTITOXIN TITER AT THE TIME OF INJECTION AND THE PROTECTION AGAINST TETANUS TOXIN

[illegible]

*The figures cited represent the amount of bonds in G-PLD as given, the figures in parentheses indicate the amounts of bonds in (the same) had occurred.

T diagnosed that in addition to being the animal had received an injection of virus from which recovered.

THE LITERARY

toxin, the animals have titers exceeding 4 units per cubic centimeter whereas 2 of 5 control animals have only 3 units. Although in 4 months the titers of the controls have fallen to 1 or 2 units, those which had received toxin have titers of from 5 to more than 15 units in 6½ months. Results in animals immunized with 0.1 and with 0.01 cubic centimeter of toxoid are similar. Such studies demonstrate that toxin in sufficient but not fatal amounts serves in the course of several months to cause a significant increase in anti-toxin titer. They do not, however, answer the question whether this response is rapid enough to increase a low titer to a protective level before the patient might succumb to natural infection with *Clostridium tetani*. Others have attempted to answer this point with somewhat confusing results.

Jones and Jamieson (20) found that a number of actively immunized guinea pigs survived a lethal spore dose but did not respond with an increase of serum antitoxin assays being made on the seventh day, and in some instances on the second, fourth, and fourteenth days. Jaulmes and Jude similarly found no increase in titer on the third, sixth, and tenth days after unimmunized guinea pigs had been given a lethal dose of spores from which they all recovered without symptoms. One explanation which leaves open the question of possible titer acceleration is that the toxin is neutralized as formed and has no opportunity of exerting antigenic activity (4, 17) Wolters and Dehmel found that two guinea pigs with low titers survived the introduction of splinters infected with a lethal dose of spores and showed increased titers on the sixth and eighteenth days. Zuger, Greenwald and Gerber concluded from experiments with guinea pigs that actively immunized animals respond to toxin with increased titers on the fourth and fifth days and to infection with spores with a delayed titer rise—a significant elevation occurring first on the 8th or 10th day. This rise seemed to occur too tardily to afford adequate protection and suggested that such a rise following natural infection in man probably cannot be relied upon to give sufficient protection. Our experiments suggest that the degree of protection against tetanus toxin depends upon the antitoxin titer at the time the toxin is administered (Table III). It appears that any increase in antitoxin which the toxin may have stimulated did not reach a sufficiently high level rapidly enough to alter the outcome, unless such a rise was almost directly proportional to the titer at the time the toxin was administered. This type of study should be extended to include inquiry into the degree of protection afforded by a given antitoxin titer induced by passive immunization as compared with the same titer resulting from active immunization. It should also be determined whether a given antitoxin titer confers the same degree of protection at a time when the titer is rising at its peak or on the decrease as well as whether it resulted from a certain dose of toxoid or from a fraction of this dose. Such studies would throw addi-

tional light upon the question whether there is some immunity conferred by toxoid other than that represented by the antitoxin in the blood. Trabattoni states that immunity may persist in guinea pigs immunized with toxoid even when the serum antitoxin is diminished or absent, which he interprets as indicative of a true tissue immunity.

The general plan of immunization consists of 2 or preferably 3 injections of toxoid given at long intervals, never less than 4 weeks, and a reinjection at the time of injury. In certain instances it may be wise to keep the titer high in advance of possible injury by administration of toxoid at intervals of 6 months or a year. For such purpose the intranasal instillation of refined toxoid (topagen) is satisfactory (13). The French army uses 3 doses of the "triple vaccine" given at 3 week intervals, the British army 2 doses of plain toxoid at 6 week intervals. The United States Army uses 3 injections of plain toxoid 3 or 4 weeks apart, a stimulating dose at the end of the first year, another during the month before departure for the zone of combat unless this takes place within 6 months of the stimulating dose, and another dose at the time of injury. The United States Navy and Marine Corps use a similar plan except that alum-precipitated toxoid is used and the basic course consists of 2 injections 4 weeks apart. The demonstration that the simultaneous injection of tetanus toxoid with diphtheria toxoid or with typhoid-paratyphoid vaccine or with both is not only feasible but actually results in a higher antitoxin titer (19, 21, 27), is an important contribution. Tetanus toxoid can be easily given during the almost universally practiced immunization against diphtheria in infants and may be given advantageously to those being immunized against typhoid fever.

Ramson (26) stated that after thousands of injections no reactions of any moment had occurred. Several anaphylactic reactions in Great Britain have been reported. Cunningham and Parish and Oakley have each reported a case of nonfatal anaphylactic shock. Whittingham stated that among 61,042 members of the Royal Air Force who were immunized, 2 had anaphylactic reactions and

12 constitutional symptoms such as malaise and fever. Seven of these had urticaria. Few reactions have been reported in this country. Jones and Moss (18) noted 2 delayed reactions consisting of local soreness and fever. Hall (15) encountered 2 urticarial reactions with the second dose of plain toxoid. Subsequently (16) he encountered one delayed urticarial reaction and 2 reactions with fever and malaise on the first injection of an alum-precipitated toxoid. On giving the second injection of this toxoid to 1,800 of these persons, 7 had fever and malaise, 4 had urticaria, and 1 had anaphylaxis. The other 500 were given another toxoid which he felt was more carefully washed, with no reactions at all. Gold (14) collected from his own experience and that of other workers 1,700 cases of patients immunized with alum-precipitated toxoid in whom there were only 2 cases of urticaria. No fatal reactions have occurred, and the reported incidence of general reactions of all sorts is surprisingly low in view of the millions of persons who have been immunized. Although there is no general agreement, investigation to date tends to link the reactions to sensitization to the Witte or Berna peptone used in the culture medium in which the organisms were grown. There is reason to have confidence in the production of purer toxin by use of other media and methods of culture from which toxoids may be prepared which will cause no reactions.

The efficacy of tetanus toxoid has been repeatedly demonstrated in laboratory animals. The present armed conflict is putting to crucial test the protection afforded in man by toxoid. Active immunization is compulsory in the French and Italian armies, and is also used in the Russian army. Though on a voluntary basis, a large part of the British army has been actively immunized. I can find a record of only a single instance of tetanus in an actively immunized person, a patient reported by Simon and Patey, who had "an essentially benign and localized form of tetanus" from which he recovered. The campaign in Flanders and the evacuation from Dunkirk gave indisputable evidence of the value of active immunization (1, 25). Ninety per cent of the British Expeditionary

Force were immunized. Each wounded man was to have been given 3 000 units of anti-toxin but because of the force of circumstances the majority of the wounded reached England without having received any anti-toxin. Among approximately 1 800 wounded men who were not immunized there were 8 cases of tetanus; there were no cases of tetanus among some 16 000 wounded who had been actively immunized.

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THE CLINICAL SIGNIFICANCE OF THE SERUM AMYLASE TEST IN THE DIAGNOSIS OF ACUTE PANCREATITIS

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IN the last few years a number of clinicians have used determinations of the level of amylase in the blood serum as an aid in the differential diagnosis of acute pancreatitis. This laboratory test has been used on the University of California Emergency Service at the San Francisco Hospital for the last 3½ years and has proved to be of considerable assistance in making a diagnosis of acute pancreatitis. In the differential diagnosis of certain other cases of acute, but obscure, abdominal disease the test has been of value in excluding the possibility of acute pancreatitis.

It is essential that the technique for the determination of serum amylase be standardized, and its accuracy confirmed repeatedly before the results can be considered significant. The normal range of serum amylase levels must be known, and their possible variations must be realized before a correct interpretation of the test can be made. We have used Somogyi's "saccharogenic" method for the determination of amylase as well as his definition of the unit. The amylolytic activity of the serum of any given normal person is usually very nearly at the same level regardless of fasting, feeding, kind of food, time of day, exercise, etc (Fig 1). Serum amylase activity in groups of normal persons is reported by most observers as being almost always within the limits of from 80 to 180 units, though Lewison reported from 40 to 175 units as the normal range in his series, and Comfort gave 320 units as the upper limit of normal. In our investigations, variations from the range between 80 and 180 units usually did not occur in normal persons, but occasionally readings below the normal limit (that is below 80 units) were found in those apparently healthy.

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A considerable elevation in serum amylase almost always occurs at some time during an episode of acute pancreatic necrosis, acute interstitial pancreatitis (acute pancreatic edema) or acute traumatic pancreatitis. Significant elevations in the amount of amylase found in the serum rarely occur except in certain phases of acute disease of the pancreas, although in certain instances acute parotitis will cause a rise in serum amylase and occasionally diseases of the kidney are accompanied by a slight elevation resulting from impaired renal excretion. Renal disease with retention of amylase is readily recognized if determinations of both serum and urinary amylase are made in all cases in which the serum amylase is only slightly increased.

In the past 3½ years, 743 amylase determinations have been made on patients on the University of California Service at the San Francisco Hospital. Most of them were made on blood serum in cases of suspected pancreatitis, or in conditions in which differentiation of pancreatitis from other acute abdominal disease was difficult. Other amylase determinations were made on bile, urine, peritoneal fluid, and fluid from cysts. The serum amylase was studied in 43 cases of acute pancreatitis. The lowest maximum reading in any single case of this disease was 225 units, the highest was 2,459 units, and the average maximum reading was 696 units. The average undoubtedly would have been higher had not a number of the patients entered late in the course of their disease when the amylase level was probably subsiding. In 35 of the 43 cases the diagnosis was acute interstitial pancreatitis (acute pancreatic edema), in 6 acute hemorrhagic pancreatitis (acute pancreatic necrosis) was diagnosed, and there were 2 cases of traumatic pancreatitis (Table I).

In more than 200 other cases of acute abdominal disease the serum amylase test was used as a diagnostic aid to rule out the possi-

TABLE I.—CASES OF ACUTE PANCREATITIS STUDIED BY THE SERUM AMYLASE TEST

	No. of cases	Confirmed by operation or autopsy	Deaths
Acute hemorrhagic pancreatitis (Pancreatic necrosis)	6	4	4
Acute interstitial pancreatitis (Pancreatic edema)	33	3	
Acute traumatic pancreatitis			
Total	41	9	5

bility of acute pancreatitis. When the amylase test is done within the first 2 or 3 days of the acute illness, a low or normal reading is of considerable value in eliminating the likelihood of acute pancreatitis.

Determinations of serum amylase were made in 42 cases of acute cholecystitis (Table II). In 14 of the 42 the additional diagnosis of acute pancreatitis was made because of high serum amylase readings and in 8 of the 14 the diagnosis was confirmed by operation or autopsy. Acute pancreatitis was diagnosed in 6 of 26 cases of chronic cholecystitis because of high serum amylase readings (Table II) and in 4 the diagnosis was confirmed at operation or autopsy. Table II shows the serum amylase values found in 12 cases of stone in the common duct. Acute pancreatitis was present in 1 of these in which the amylase level was 1,875 units.

The following case reports are examples of the 3 main types of proved acute pancreatitis that show great elevations in the serum amylase level, namely pancreatic necrosis interstitial and traumatic pancreatitis.

CASE. A housewife 38 years of age complained of severe epigastric pain radiating to the back, associated with nausea and vomiting of 8 days' duration. There had been no previous attacks and there was no history of alcoholism. She appeared to be acutely ill. The abdomen was distended, there was ecchymosis in the flanks and Cullen's sign was present. A large tender mass was palpated in the epigastrium. The temperature was 101.5 degrees, the pulse rate 114 and the white blood count 12,000, with 90 per cent polymorphonuclear cells. Urinalysis showed trace of albumin and slight glycosuria. The serum amylase was 22,158 units the eighth day of the illness. The icterus index was 32. The patient's temperature ranged between 100 and 103 degrees. On several occasions she developed profound shock associated with cyanosis from which she recovered temporarily following trans-

TABLE II.—SERUM AMYLASE IN DISEASE OF THE GALLBLADDER AND BILE DUCTS

Disease	Serum amylase u-ls	Serum amylase ls-ls	Deaths over 100	Total Cases
Acute cholecystitis	6		14	47
Chronic cholecystitis	7	5	6	26
Common duct stone	3	6	—	8
Total	28	33		

fusions of blood. On the tenth day of the disease the epigastric mass was drained through a small midline incision, under local anesthesia. A considerable amount of hemorrhagic fluid was found together with necrosis of 1 and acute hemorrhagic necrosis of the pancreas. The patient died on the eleventh day. At a postmortem acute pancreatic necrosis and fatty degeneration of the liver were found. The gall bladder and bile ducts were normal.

CASE. A housewife 43 years of age had pain in the epigastrium and right upper quadrant of the abdomen with vomiting of 24 hours' duration. She had had a similar attack weeks previously. There was no history of alcoholism. Tenderness, spasm and rebound tenderness were present throughout the entire abdomen but were most marked in the right upper quadrant. The temperature was 101 degrees, the pulse rate 104 and the white blood count 12,000, with 98 per cent polymorphonuclear cells. The only abnormal finding on urinalysis was faint trace of albumin. The level of the serum amylase was not determined at this time. The diagnosis was acute cholecystitis. At operation the gall bladder was found to be normal but the pancreas was indurated and edematous. The serum amylase was 205 units on the first postoperative day. The convalescence was uneventful. Subsequently the patient had numerous episodes of mild abdominal pain. A very severe attack of epigastric pain occurred about 3 years later and, after 24 hours, she entered the hospital again. She appeared acutely ill. The abdomen was tender and spastic throughout with most marked findings in the epigastrium and right upper quadrant. The temperature was 100 degrees, the pulse rate 100 and the white blood count 12,000, with 8 per cent polymorphonuclear cells. Urinalysis showed faint trace of albumin. The serum amylase was 1,500 units on the first day and 650 units on the third day. The attack subsided spontaneously.

CASE 3. A boy 9 years of age hit by an automobile fell to the street striking his left side about 1 hour before he entered the hospital. He complained of severe pain in the left upper abdominal quadrant. There was no radiation of pain and no vomiting. Tenderness, rebound tenderness, and spasm were present in the left upper abdominal quadrant. The temperature was 101.6 degrees, pulse rate 120, and blood pressure 90/80. A blood count showed 12,000 white blood cells, with 55 per cent polymorphonuclears, 80 per cent hemoglobin, and 4,800,000 red blood cells. During 4 hours' observation, the abdominal findings increased somewhat in severity.

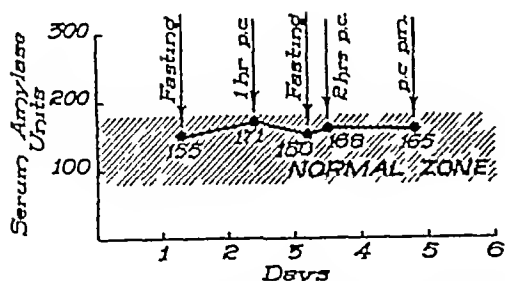


Fig 1 This graph indicates the results of a series of serum amylase determinations taken on a normal person at various times over a period of 4 days. The readings are very nearly the same regardless of fasting, feeding, time of day, etc. The shaded area designated as "normal zone" represents the usual range of variations of normal serum amylase levels in a group of normal persons.

The serum amylase level was 2,117 units. The diagnosis was traumatic rupture of the spleen and traumatic pancreatitis. At operation, a large amount of bloody fluid was found in the peritoneal cavity. The spleen was found to have been lacerated and was removed. The tail of the pancreas was edematous and hemorrhagic. The patient recovered.

Several types of variations that may occur in the serum amylase level during an episode of acute pancreatitis must likewise be considered. In order to understand these variations a number of patients were studied over a period of several days and serum amylase determinations were made at intervals of from 8 to 12 hours. At the same time, an attempt was made to correlate the clinical course of the acute pancreatic disease with the variations in serum amylase. In this study we noted 6 types of variation of the serum amylase level in acute pancreatitis: (1) sharp rise and fall to normal, (2) sharp rise and fall to subnormal, (3) fluctuations (following the clinical subsidence of acute pancreatitis), (4) sustained high levels, (5) secondary elevations, and (6) slight increases.

In the following discussion a case report is given to illustrate each type.

1 Sharp rise and fall to normal. A sharp rise in serum amylase almost always occurs within a few hours after the onset of acute pancreatic disease, and the level usually remains elevated for from 24 to 72 hours, and then declines sharply into the normal zone (Fig 2). The height of the rise of the serum amylase level during an episode of acute pancreatitis does not necessarily reflect the severity or indicate the type of the acute pan-

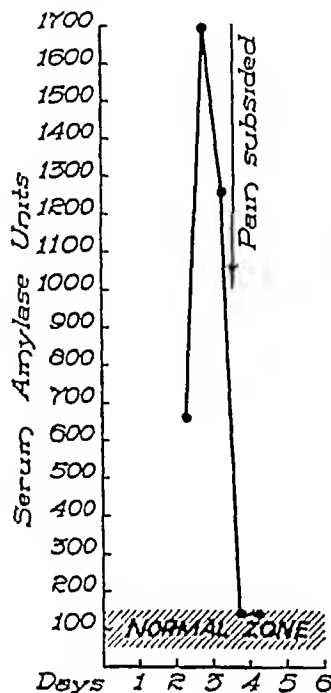


Fig 2 (Case 4, male, aged 38) Sharp rise and fall of the serum amylase level in a case of transient acute interstitial pancreatitis associated with acute alcoholism.

creatic disease. The declination in the curve does not always correspond exactly to the subsidence of the acute process, but often it does in the acute interstitial type of pancreatitis. Occasionally the level of serum amylolytic activity declines more gradually than usual following an attack of acute pancreatitis. As far as we know at the present time, this latter finding is of no particular significance.

CASE 4. A man 38 years of age had been drinking considerable quantities of alcohol for several days before the onset of his illness. For about 48 hours prior to his entry into the hospital he had had severe burning epigastric pain radiating to the back. He vomited once. There had been a similar attack 3 years before. His abdomen was tender throughout with maximum tenderness in the epigastrium and some spasm in the same region. His temperature was 99.6 degrees and pulse rate 68. Urinalysis showed a trace of albumin but no sugar. The white blood count was 26,200 with 89 per cent polymorphonuclear cells. Serum amylase studies were taken twice daily (Fig 2). The pain and tenderness had subsided completely by the day after entry to the hospital but slight spasm remained in the epigas-

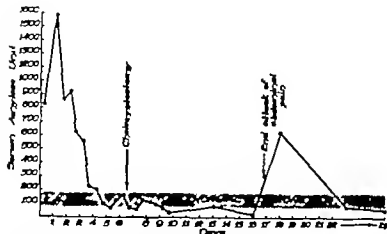


Fig. 3 (Case 5, female, aged 60 years.) Sharp rise and fall into the subnormal zone of the serum amylase level in case of acute cholecystitis and acute pancreatitis. A second attack of abdominal pain on the seventeenth day of hospitalization was accompanied by second elevation in the serum amylase level.

trium. On the third day the patient had no symptoms or signs of his disease and left the hospital.

2 Sharp rise and fall to subnormal level. The final explanation of the dip below the normal zone that sometimes occurs in acute pancreatitis has not been made although most observers believe that the extremely low levels correspond to episodes of impairment of hepatic function. The possibility that the normal zone of serum amylase activity should be reduced to include lower readings (below 80 units) must also be considered.

CASE 5. A woman 60 years of age complained of aching pain in the right upper quadrant, radiating to the tip of the right scapula, with nausea and vomiting of 12 hours duration. She gave history of



Fig. 4 (Case 6, male, aged 30 years.) The graph of serum amylase levels in this case of acute interstitial pancreatitis associated with acute alcoholism demonstrates the fluctuations above and below as well as within the usual normal zone, that sometimes occur following the subsidence of an attack of acute pancreatitis.

chronic cholecystitis with many episodes of colic for 40 years. She was very obese and acutely ill. The abdomen was moderately distended and guarding and tenderness were noted in the epigastrium and right upper quadrant. Her temperature ranged from 100 to 101 degrees and her pulse rate from 90 to 110. The white blood cell count was 8,600. The patient appeared to improve but because of the severe tenderness remaining in the right upper quadrant a cut cholecystitis was suspected. Cholecystectomy was done under local anesthesia. The gall bladder was inflamed and contained calculi. The amylase, the peritoneal fluid was 805 units and that in the bile 70 units. The amylase levels in the blood serum are shown in Figure 3. On the seventeenth day after entry the patient had a second attack of moderately severe pain and tenderness in the right upper quadrant that subsided within 48 hours. Cholangiography showed a calculus at the lower end of the common duct.

Case 9 (Fig. 7) also illustrates this fall of the serum amylase level below the normal zone following an attack of acute pancreatitis.

3 Fluctuations within the normal zone and slightly above and below the usual normal range (from 80 to 180 units) occur rather frequently during the days following an episode of acute pancreatitis. At present, the significance of these fluctuations is unknown. The subnormal readings mentioned are often a part of this fluctuating curve as may be seen in Figure 4.

CASE 6. A brewer 30 years of age gave history of drinking very large amounts of alcohol for a period

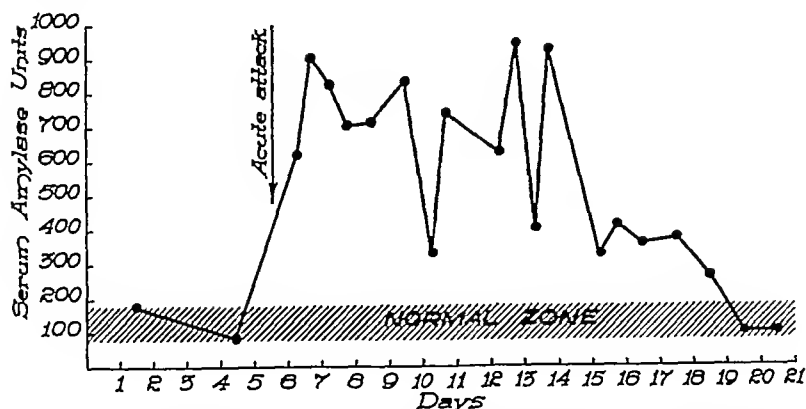


Fig 5 (Case 7, male, aged 49 years) Sustained high amylase levels in a case of acute cholecystitis and acute pancreatitis. In this case the serum amylase remained elevated for 4 or 5 days following the subsidence of signs of acute pancreatitis. Sustained high amylase levels are more often associated with a continuation, extension, or progression of acute pancreatitis.

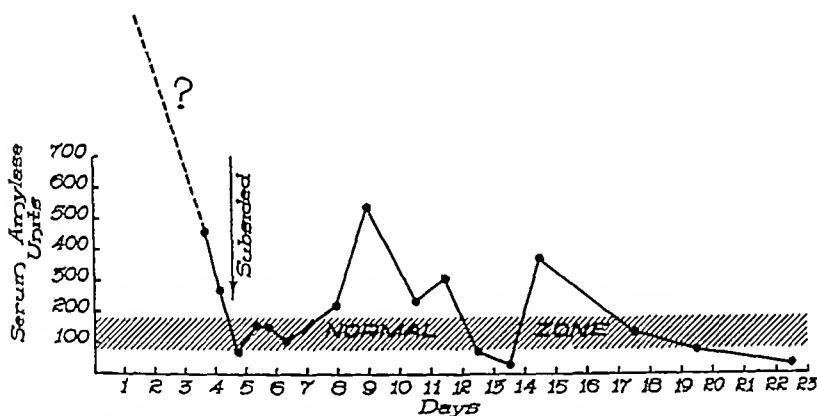


Fig 6 (Case 8, male, aged 47 years) Moderately high secondary rise in serum amylase level that developed following the subsidence of the signs and symptoms of an attack of acute pancreatitis. In this case there were no symptoms or signs of exacerbation of acute pancreatitis to correspond to the secondary rises in serum amylase.

of 1 month. He entered the hospital complaining of severe and constant epigastric pain associated with nausea and vomiting of 18 hours' duration. The abdomen was obese and spasm and tenderness were noted in the upper part of the abdomen. The temperature was 101.6 degrees and the pulse rate 116. The white blood count was 17,300, with 80 per cent polymorphonuclear cells. The urinalysis showed a trace of albumin but no sugar. The serum amylase levels are shown in Figure 4. The pain and abdominal findings subsided in 24 hours, but fever and vomiting continued for several more days.

4. Sustained high amylase levels may be associated with a continuation, extension, or progression of acute pancreatitis, or with

acute exacerbations of pancreatitis occurring at very frequent intervals. Case 7 demonstrates sustained high amylase values.

CASE 7. A man 49 years of age complained of cramping pain which began in the left upper quadrant and radiated to the left shoulder and back. He was nauseated and vomited several times. There was a history of chronic cholecystitis and occasional episodes of severe colic in the left upper quadrant, of 10 years' duration. There was no history of alcoholism. The patient was jaundiced, the abdomen was moderately distended and there was tenderness in the entire upper part of the abdomen, most marked in the epigastrium. The temperature was 98.6 degrees and the pulse rate was 100 on entry. Blood

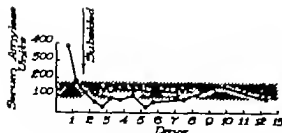


Fig. 7 (Case 9, female, aged 69 years) In this case in which the clinical signs and symptoms are rather typical of acute pancreatitis, the slight elevation in serum amylase is somewhat confirmatory of acute pancreatitis. This graph also shows the dip below the normal zone of serum amylolytic activity that sometimes follows an attack of acute pancreatitis.

count showed 7,600 white blood cells, with 68 per cent polymorphonuclears. The urine contained bile but was otherwise negative. On the morning of the seventh day after entry the patient had severe pain in the left upper quadrant with nausea, vomiting, and epigastric tenderness. The white blood count was 8,100 and urinalysis showed a heavy trace of albumin. The serum amylase readings are shown in Figure 5. The diagnosis was acute pancreatitis and acute and chronic cholecystitis with icterus. The acute abdominal symptoms and signs subsided over the next 3 days, but the amylase level remained elevated for more than a week and gradually declined into the normal zone (Fig. 5). Operation was performed during quiescent period. The gall bladder was still somewhat inflamed and edematous and contained many calculi, the common duct was enlarged and contained a large soft stone and the pancreas was enlarged and indurated.

5 *Acute exacerbations of pancreatitis* are often reflected in the graphic curves of serum amylase readings as secondary elevations when the patient has had more than one episode of acute pancreatitis while under observation. Case 5 (Fig. 3) serves as an example of a case of acute pancreatitis in which there was an exacerbation of the disease while the patient was in the hospital. Occasionally these secondary rises in the level of serum amylase follow a few days after an attack of acute pancreatitis without subjective or other objective findings indicative of an exacerbation of the disease. After the subsidence of an episode of acute pancreatitis, a rise in the serum amylase, not necessarily accompanied by abdominal pain, may be caused by the manipulation of the pancreas that sometimes occurs during the course of surgical procedures on the bile duct.

CASE 8 A man 47 years of age complained of severe epigastric pain and vomiting of 4 days duration. He had had no abdominal pain or indigestion previously. He had used alcohol many years before but more recently. The abdomen was moderately distended and generalized tenderness and spasm were most marked around the umbilicus. The temperature was 100 degrees and the pulse rate 80. The white blood count was 5,400, with 87 per cent polymorphonuclear cells. The urinalysis was negative. The abdominal pain and tenderness subsided over period of 3 days and the patient remained free from symptoms thereafter during his hospitalization. The serum amylase level, however, rose to 530 units on the ninth day though there were no symptoms or signs of disease at that time (Fig. 6). Operation was performed during a quiescent period. Mild chronic cholecystitis and edema and induration of the entire pancreas were found. Cholecystectomy was done.

6 *Slight increases in the serum amylase* are of relatively less diagnostic value than are the moderate or large increases that usually accompany the early course of acute pancreatitis. Slight elevations in serum amylase however may be considered as somewhat more significant when they are found in patients who present themselves late in the course of acute pancreatic disease or just after the subsidence of a typical episode of acute abdominal pain. Case 9 is illustrative.

CASE 9 A woman 69 years of age complained of severe epigastric pain and vomiting of 24 hours duration. She had had no abdominal discomfort previously and there was no history of alcoholism. Marked tenderness was present in the epigastrium. The temperature was 100 degrees and the pulse rate 90. The blood count showed 7,700 white blood cells, with 90 per cent polymorphonuclears. The urine showed a trace of albumin. The pain and tenderness subsided completely over the ensuing 4 hours. The gall bladder visualized normally by cholecystography. Figure 7 shows the serum amylase determinations.

If the clinical picture is less typical of acute pancreatitis, these slightly increased serum amylase readings must be considered equivocal. This is seen in Case 10.

CASE 10 A woman 63 years of age complained of severe pain in the right upper quadrant, with nausea and vomiting of 4 days duration. She was not particularly ill. Her previous history suggested chronic cholecystitis of many years duration. She used alcohol occasionally. There was tenderness throughout the entire abdomen, most marked in the upper right quadrant where spasm was also present. The temperature was 99 degrees and the pulse rate 70.

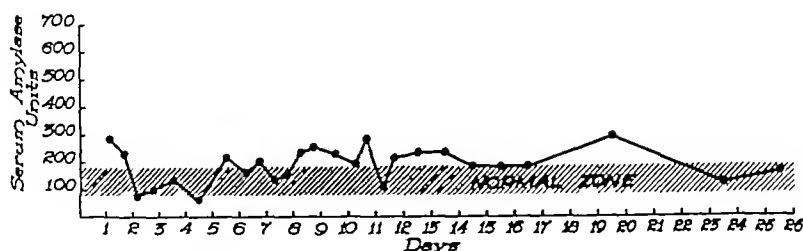


Fig 8 (Case 10, female, aged 63 years) The slight elevations in the serum amylase level are of relatively less confirmatory value in this case in which the clinical findings are not typical of acute pancreatitis

Blood count showed 9,300 white cells with 86 per cent polymorphonuclears. The urine showed a trace of albumin but no sugar. The symptoms and signs of illness subsided over a period of 3 days. The gall bladder was visualized normally by cholecystography. The serum amylase readings are shown in Figure 8.

SUMMARY

The laboratory determination of the serum amylase is a valuable diagnostic test in acute disease of the pancreas. Moderate to marked elevations in serum amylase activity occurring early in the course of an acutely painful abdominal condition offer confirmatory evidence of acute pancreatitis. The serum amylase test is also of some value in the recognition of acute pancreatitis occurring as a complication of cholecystitis or disease of the bile ducts.

The limitations and possible variations of the test for serum amylase must be known

before its diagnostic value can be realized. Within these limitations the test may often be of considerable assistance to the surgeon. Six variations that may occur in the serum amylase during, and immediately after, an episode of acute pancreatitis are described.

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THE EFFECT OF DISTENTION OF THE SMALL INTESTINE ANOXEMIA AND OXYGEN THERAPY UPON THE FLOW OF BILE AND URINE IN THE DOG

Relationship to the Hepatorenal Syndrome

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THERE has been much speculation as to the cause of the combined failure of liver and kidney function and degeneration in some cases of intestinal obstruction, peritonitis, hyperthyroidism and burns. We have tried, therefore to investigate the possible existence of a physiological basis for the occurrence of the hepatorenal syndrome in these conditions.

We first studied the effect of distention of the entire small intestine upon the flow of bile and urine. These experiments were performed upon 10 dogs fasted for 18 hours and anesthetized with sodium pentobarbital (30 milligrams per kilogram of body weight intravenously). The blood pressure was recorded from the cannulated left carotid artery. The respiration was recorded from a bellows around the chest of the dog. Bile flow was studied in 7 dogs by cannulating the common bile duct close to the duodenum after ligation of the cystic duct near the common duct. The drops of bile were recorded by an electrical recorder. A ligature was placed around the duodenum and a large cannula was tied into the terminal ileum which was also ligated distal to the cannula. The cannula was attached to a mercury manometer and an inflation bulb by means of a Y tube. The abdominal wall was closed with heavy silk suture. A control basal flow of bile was then obtained after an interval of about 30 minutes.

Intestinal distention was maintained at pressures of 20, 40 and 70 millimeters of mercury for a period of 30 minutes each. Oxygen was administered by means of a nasal

catheter to determine what effect it had upon the bile flow with the intestine distended to pressures amounting to 40 and 70 millimeters of mercury.

The excretion of urine was studied in a similar manner upon 3 dogs. Each ureter was cannulated and the flow of urine was recorded on a revolving kymograph drum by electrical recorders. A uniform mild diuretic was maintained by the continuous intravenous drip administration of 1000 cubic centimeters of physiologic sodium chloride solution over a period of 4 hours. In all of the experiments, especial care was taken to avoid the kinking of the cannulas when the intestine was distended.

Results. Intraenteric pressures of 20 and 40 millimeters of mercury resulted in a decrease in the bile flow of 7 to 42 per cent below the control level in 6 of the 7 dogs (Table I). Dog 6 showed no change. These pressures are comparable to intraenteric pressures in human cases of intestinal obstruction reported by Wangenstein. Since higher pressures may occur in some clinical cases of intestinal obstruction we distended the intestine to a pressure of 70 millimeters of mercury and found a further decrease in the bile flow in 4 dogs. Oxygen therapy lessened this inhibition in all of the dogs treated.

Nervous reflex inhibition of the flow of urine did not occur upon distention of the small intestines to pressures of 20, 40, 60, and 90 millimeters of mercury. An increase in the urine flow from 11 to 8 per cent occurred (Table II). This was attributed to an increased blood flow through the kidneys.

The blood pressure in each instance was not significantly altered by distention of the small intestine.

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TABLE I —EFFECT OF ACUTE INTESTINAL DISTENTION UPON THE FLOW OF BILE IN THE NEMBUTALIZED DOG

Dog No	Intraenteric pressure in millimeters of mercury				
	20 Per cent	40 Per cent	70 Per cent	70 plus oxygen Per cent	Control after release of pressure Per cent
1	-16	+5	+5		-16
2	-20	-6	-26		-36
3	-15	-15	-30		-30
4	-16	-22	-16	-5	
5	-28	-42	-38	-23	
6	0	0	-15	0	
7	-7	-14	-42	-7	0

The depth of respiration was decreased and the rate was increased by distention. Oxygen therapy decreased the respiratory rate and lessened the depression of bile flow produced by distention of the small intestine.

The second part of this investigation was concerned with the effect of anoxemia upon bile and urine flow in 10 nembutalized dogs. The blood pressure, respiration, and the flow of bile and urine were recorded upon each dog as previously described. Mixtures of 5, 10, 15, and 20 per cent oxygen with nitrogen and 100 per cent oxygen were administered by a Heidbrink gas machine. Each mixture was breathed for 30 minutes before and during the time that a tracing was taken. Five per cent oxygen was given as long as the animal could tolerate it. This was usually found to be 5 to 10 minutes.

Results Inhalation of 15 per cent oxygen in nitrogen for 30 to 45 minutes resulted in a 16

TABLE II —EFFECT OF ACUTE INTESTINAL DISTENTION UPON THE SECRETION OF URINE IN THE NEMBUTALIZED DOG

Dog No	Intraenteric pressure in millimeters of mercury				
	20 Per cent	40 Per cent	60 Per cent	90 Per cent	Control after release of pressure Per cent
1	+11	+26	+50	+81	-12
2	+120	+100	+360	+80	+80
3	+57	-18	+12		-14

TABLE III —EFFECT OF INHALATION OF VARIOUS OXYGEN CONCENTRATIONS UPON THE FLOW OF BILE IN THE NEMBUTALIZED DOG

Dog	Per cent oxygen inhaled for one half hour			
	15 Per cent	10 Per cent	5 Per cent	100 Per cent
1	-25	-75	-62	0
2	-18	-31	-100	-87
3	+10	-24	-52	
4	0	-20	-100	0
5	-31	-47	-73	+21
6	-16	-38	-65	-17
7	-20	-46	-86	
8	-50	-46	-93	-26
9	-21	-26	-33	-21
10	-20	-66	-73	-33

to 50 per cent decrease in the flow of bile below normal and a 13 to 69 per cent decrease in the flow of urine below normal in 10 nembutalized dogs (Tables III and IV).

Inhalation of mixtures of 10 and 5 per cent oxygen with nitrogen caused a further decrease in the flow of bile and urine. Acholia developed in 2 dogs and anuria was noted in 5 dogs.

The inhalation of 100 per cent oxygen for 30 to 45 minutes after the anoxemia resulted in an increase in the flow of bile and urine above that which was observed during the anoxemia,

TABLE IV —EFFECT OF INHALATION OF VARIOUS OXYGEN CONCENTRATIONS UPON THE FLOW OF URINE IN THE NEMBUTALIZED DOG

Dog	Per cent oxygen inhaled for one half hour			
	15 Per cent	10 Per cent	5 Per cent	100 Per cent
1	-45	-80	-87	-20
2	-64	-72	-100	-61
3	-69	-71	-89	
4	-52	-70	-63	-19
5	-56	-74	-87	-68
6	-33	-16	-100	-8
7	-66	-75	-100	
8	-13	-73	-100	+5
9	-38	-57	-69	-42
10	-30	-100	-100	+33

in 3 dogs the flow was increased above the normal control level.

SUMMARY

The results of our investigations so far indicate that there is a physiological basis for the combined failure of liver and kidney function in some cases of intestinal obstruction. Liver function is first impaired by a nerve reflex inhibition due to distention of the intestine.

The anoxemia present in cases of severe intestinal distention, hyperthyroidism and

burns may produce a marked decrease in the formation of bile and urine. If mild this may be a predisposing cause making the liver and kidneys more susceptible to other injurious agents. In some instances in which the anoxemia is severe, it may be the primary factor responsible for the combined failure of liver and kidney function and in some instances may produce an acholia and anuria.

Inhalations of high concentrations of oxygen are indicated when anoxemia is suspected as a factor in cases of unpaired liver and kidney function.

PRINCIPLES OF PLASTIC SURGERY IN THE TREATMENT OF MALIGNANT TUMORS OF THE FACE

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MALIGNANT tumors of the skin occur most frequently on the exposed areas of the body, especially on the face, therefore, the appearance of the lesion or the increase in the size of a long standing cutaneous growth is recognized by the patient early in the course of the disease. However, the pathway open to him is an uncertain one, since there is conflict of professional opinion as to the ideal method of treatment for malignant lesions of the skin. Fear of facial disfigurement as a result of treatment is uppermost in the mind of the patient. Undoubtedly it is due to these factors that a high percentage of malignancies of the face are recurrent lesions when they are presented for surgical excision. In the management of the slowly growing, nonmetastasizing basal cell carcinoma of the skin, as well as in the more rapidly developing and metastasizing epidermoid carcinoma, the responsibility of the profession is great, for the vast majority of these lesions are curable if treated by an adequate method early in the course of the disease. If allowed to invade the bony structures of the face and head, they may be the cause of death. Therefore, it must be clear that the cardinal principle of any treatment which may be employed with safety is the complete destruction of the lesion. The general practitioner, in his advice to the patient with an early malignant tumor, must select one of four methods of therapy: electrodesiccation, x-ray therapy, radium therapy, or primary surgical extirpation. Reports in the literature concerning recurrent carcinoma of the skin indicate that the percentage of recurrence following electrodesiccation is sufficiently high to justify condemnation of this treatment. Although x-ray treatment is an

efficient method of dealing with basal cell carcinomas, especially since it does not entail hospitalization and leaves minimal disfigurement, it has the disadvantages that therapy must be planned upon information obtained from biopsy and the entire growth is not available for microscopic study. Also the scarring of soft tissues produced by the ray may make it difficult to recognize a recurrence. Radium therapy has many of the same advantages and disadvantages as has x-ray therapy. The deforming scar which follows radium therapy often necessitates subsequent plastic excision. Surgery alone offers the satisfaction of complete extirpation of the malignant lesion and, in addition, the specimen is available for microscopic determination of the extent of its invasion. The single objection to surgery is the problem presented in the satisfactory restoration of the contour of the face—the appearance of the patient. If the removal of a malignant tumor of the face results in serious disfigurement, the patient is confronted with new difficulties, both economic and psychic, such as the loss of his job, or the development of an inferiority complex due to self-consciousness of his deformity. It is the object of this presentation to point out that, with a knowledge of the principles of plastic surgery, malignant tumors of the face can be treated successfully by surgery when first diagnosed and that the final cosmetic result is equal to or better than that of any other method. There is the additional satisfaction of knowing that the lesion has been removed completely. Once the lesion recurs following adequate primary irradiation, radical surgical extirpation certainly is justified. In this presentation certain principles of plastic surgery will be emphasized which come into play in the treatment of malignant lesions of the face and the subsequent restoration of appearance and function. If utilized by surgeons, they serve to place a high percentage

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of carcinomas of the face in the group which can be treated satisfactorily by surgery. If carcinoma of the face is to be dealt with by the surgeon, he should be familiar with and adhere to the following principles:

1. Generous estimate in advance, of the tissue which must be removed with the lesion.
2. Consideration of Langer's lines of elasticity of the skin in planning the incision.
3. Use of the temporary Thiersch graft.
4. Indications for the use of free grafts of skin, derma, fat, fascia, cartilage and bone.
5. Use of pedunculated flaps.
6. Indications for the use of prostheses.

STATISTICS

From September 1932 to September 1940 exactly 100 patients were treated by surgery at the New York Hospital for malignancy of the skin of the face and neck. A histological classification of these tumors of the skin of the face and neck is presented in Table I.

TABLE I.—HISTOLOGICAL CLASSIFICATION

	Cases
Basal cell carcinoma	40
Recurrent basal cell carcinoma	4
Recurrent basal cell carcinoma invading bone	
Epidermoid carcinoma	
Recurrent epidermoid carcinoma	7
Epidermoid carcinoma invading bone	
Recurrent epidermoid carcinoma invading bone	
Epidermoid carcinoma of lip	
Melanosarcoma	4
Salivary gland carcinoma	3
Epithelioma adenoides cysticum	
Fibrosarcoma	
Fibrosarcoma invading bone	
Metastatic carcinoma from thyroid	
Adenanthoma invading skin	

Basal cell carcinoma. It should be stated here that it is not a fixed policy to treat all basal cell carcinomas of the skin by surgical excision. X-ray therapy is an efficient method of dealing with these growths and may be carried out without the expense of hospitalization. Thus no time is lost from work and the therapy is effective with minimal facial disfigurement. However it is interesting to note in a study of the 40 cases of basal cell carcinoma that primary surgical excision in tumors of the skin is as effective as x-ray and that the cosmetic results compare favorably with any other method. The follow-up on

these cases shows that out of 40 there was only 1 which recurred following primary surgical excision. Thirty nine cases are free from disease 3 1/2 years after operation. The rate of survival for 3 years without disease, therefore, is 94.7 per cent. The 5 year disease free survival rate is 90 per cent. The method of surgical treatment employed in these cases was as follows: simple excision, 30 cases; excision and thick split graft, 9 cases; excision and whole thickness graft, 11 cases. The anatomical distribution of the lesions in these 40 cases was as follows: on the nose, 11 cases; cheek, 9; neck, 5; eyelid, 5; chin, 3; ear, 3; temple, 1; forehead, 2; lip, 1.

Epidermoid carcinoma. Because of the high degree of malignancy of the epidermoid carcinomas and their tendency to metastasize surgery is advised for them as a primary method of treatment. In the period of time covered by this survey, 12 cases of epidermoid carcinoma of the skin of the face and neck were treated by primary surgical excision. Anatomically these were distributed as follows: 3 cases of the ear, 3 of the nose, 2 of the cheek, 3 of the temple, 1 of the eyelids. The methods of surgical treatment were as follows: simple excision in 8 cases; excision and whole thickness graft in 1 case; excision and thick graft in 2 cases; excision and sliding flap in 1 case.

Metastatic cervical glands have been removed by block dissection or treated by x-ray therapy. Three of these patients were operated upon sufficiently long ago to be reported as 3 year cures. The follow-up at the present time shows that with the exception of 1 patient who died of heart disease 1 year after operation, all are free from disease at an average time of 1 1/4 years after operation.

Recurrent basal cell carcinoma. In this interesting group there are 15 cases including 1 in which the recurrent growth had invaded the frontal bone. The previous treatment received by these patients is listed as follows:

	Cases
X-ray therapy adequate dosage	4
X-ray therapy amount unknown	
Radium therapy amount unknown	3
Destruction	
Electric needle	
Surgical excision	
Cauterization	
Method of therapy unknown	

TABLE II—MALIGNANCY OF THE FACE INVOLVING THE BONE

Case	Lesion	Operative treatment	Result
1	Sarcoma invading maxilla	Resection of maxilla temporal flap	Well after 3 years
2	Squamous cell carcinoma invading maxilla	Resection of maxilla temporal flap	Well after 4 years
3	Recurrent basal cell carcinoma invading frontal bone	Resection of frontal bone and upper eyelid scalp flap	Well after 8 years
4	Recurrent fibrosarcoma invading mastoid bone	Excision of tumor and external ear cauterization of bone prosthesis	Well after 2 years
5	Recurrent adamantinoma of mandible invading skin	Resection of mandible with parotid gland and sacrifice of facial nerve prosthesis	Well after 1 year
6	Recurrent epidermoid carcinoma invading orbit and temporal bone	Extirpation of orbit resection of orbital bones	Died 8 months after operation of direct extension of lesion to brain and distant metastases
7	Recurrent epidermoid carcinoma invading skull	Resection of portion of parietal and frontal bones over sagittal sinus thick split graft	Died 5 days after operation of meningitis and septicemia

The anatomical distribution of the lesions in these cases was as follows: 5 of the nose, 4 of the cheek, 3 of the eyelid, 1 of the temple, 1 of the forehead, 1 of the neck. The surgical treatment in the management of these recurrent lesions was as follows: excision, 2 cases, excision and thick split graft, 6, excision and whole thickness graft, 3, excision and sliding flap, 3, excision, sliding flap, and resection of frontal bone, 1 case. In all but 1 of these 15 recurrent tumors the primary treatment was other than surgery and in 12, or 80 per cent, the secondary radical excision gave a good clinical result. One tumor recurred 1 year after and another 6 years after radical surgical excision. A third patient could not be followed. Of the remaining 12 patients all are free from disease for periods varying from 1 to 8 years. Eight patients were operated upon sufficiently long ago to be reported as 3 year cures, 2 as 5 year cures, the percentage of 3 year cures, then, is 90, of 5 year cures, 66. These figures serve to emphasize the seriousness of recurrent basal cell carcinoma of the face. It is unfortunate that the primary treatment of these relatively benign lesions of the skin is inadequate so often. The most likely explanation of the situation is that simple methods of therapy afford cures in a high percentage of cases, the potential danger of these early lesions is not sufficiently emphasized, and there is a tendency on the part of both physicians and surgeons to be hesitant in recommending surgery in facial tumors because of the fear of disfigurement from postoperative scars.

Recurrent epidermoid carcinoma This group includes 9 cases, in 2 of which the recurrent lesion had invaded the underlying bone. The primary treatment in these cases was as follows:

	Cases
X ray therapy, adequate dosage	2
X ray therapy, amount unknown	3
Cauterization	2
Desiccation	1
Radium therapy	1

The anatomical distribution of the lesions was as follows: 3 cases of the neck, 3 of the eyelids, 1 of the forehead, 2 of the scalp. Extensive surgical resection was necessary in all of these cases and the surgical treatment comprised excision in 3 cases, excision and whole thickness graft in 2, excision and thick split graft in 1, excision and prosthesis in 1, excision, resection of skull, and thick split graft in 1, excision, resection of orbital bone, thick split graft in 1. Seven of these patients (78 per cent) survived operation and have been free from disease for a period of time varying from 1 to 7 years. One patient died 1 year after extirpation of the orbit and removal of a portion of the temporal and orbital bones. There was 1 postoperative death following excision of a portion of the skull for infected carcinoma of the scalp. The fact that this was a case in which it was necessary to carry out extensive resection of bone calls attention to the increased danger of radical excision when the growth has invaded bone.

There were 7 cases in which the lesion of the face had involved the bone. These are listed in Table II.

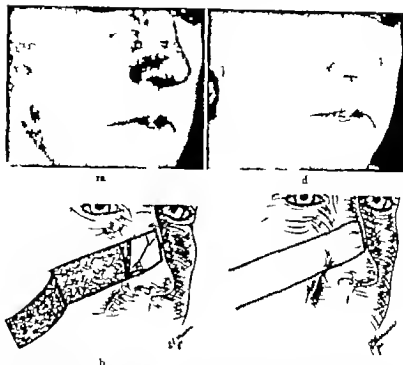


Fig 1. Case a. Basal cell carcinoma of the nose, twice recurrent. Excision and primary closure as done by means of sliding flap from the cheek as shown in b and d. The appearance 9 months after operation. Follow up examination 3 years and 4 months later showed no recurrence.



Fig 2. Case a. Basal cell carcinoma of the nose. The lesion had recurred once following cauterization and twice following courses of ray therapy. Such cases are presumed to be adequate. b. Shows the extent of the bone thickness

graft needed for replacement. Graft as taken from the cervical region. c. The appearance of the nose 4 years after operation as performed. No recurrence had occurred 4 years later.

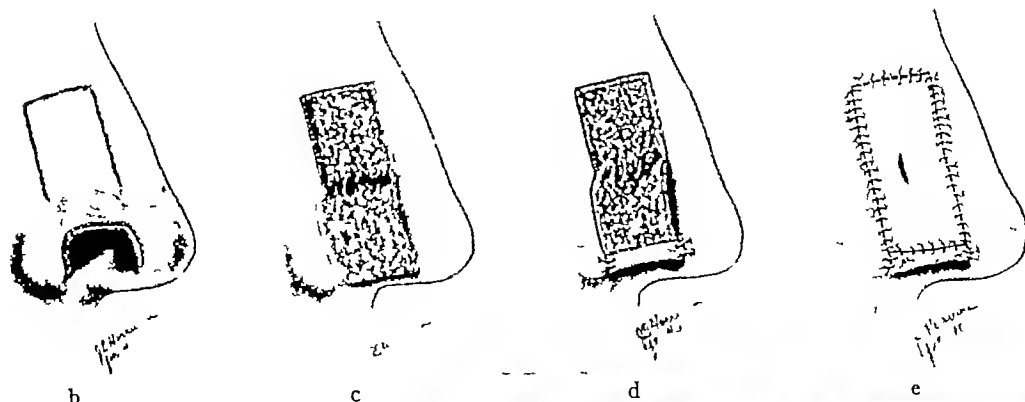


Fig 3 Case 3 a, Tumor of the skin and cartilage of the nose in a 32 year old man, the tumor proved to be metastatic from carcinoma of the thyroid b, c, d, e, Show the steps involved in primary reconstruction of the nose after through and through resection of the skin, alar cartilage, and mucous membrane b, The outline of a flap of skin from the upper portion of the nose The epithelium was excised from the region inferior to the flap as indicated by the dotted area c, The flap is swung downward to line the nose d, The distal end of the flap of skin has been turned back on itself to provide a smooth cutaneous margin for the nostril e, A whole thickness graft sutured in place over the raw area f, The postoperative result Examination 1 year after operation showed no recurrence in the nasal region though the patient is still receiving x ray therapy to the cervical and thoracic regions



The first and third cases in the above list will be referred to later in this report as Cases 5 and 4, respectively The 2 deaths listed above have been recorded previously in the discussion of recurrent epidermoid carcinoma

CASE REPORTS

Case 1 illustrates the use of sliding flaps from the neighborhood to cover the defect of soft tissue after excision of malignant tumor

Case 1 A W, New York Hospital No 208378, a 57 year old woman, presented herself for treatment of an infiltrating lesion of the right side of the nose which was noticed for the first time 10 years before admission and which had recurred following 2 surgical excisions performed in another institution 9 and 5 years ago Rectangular excision of this recurrent basal cell carcinoma was done and the defect was closed by means of a sliding flap of skin and subcutaneous tissue as shown in Figure 1 No recurrence $3\frac{1}{2}$ years later

Free grafts of skin which are available for the repair of defects created by surgical ex-

cision of malignant tumors of the skin of the face include the following (1) the Ollier-Thiersch graft or razor graft (3), (2) the thick split graft (1), (3) the three-quarter thickness or intermediate graft (5), and (4) the whole thickness graft (2) The chief value of the Ollier-Thiersch graft lies in the fact that its epithelial surface affords cutaneous healing of the wound after excision of a growth and scar formation is prevented However, the appearance of the grafted area is unsatisfactory Therefore, the use of such grafts on the face as a final measure is condemned As a temporary method this thin graft allows for observation of the operation site for recurrence of the tumor and affords time for the preparation of a suitable flap of soft tissue The term "temporary Thiersch graft" has been coined to describe this graft, the material available for it is nearly inexhaustible for it is readily obtained from the thigh or torso The thick split graft and the intermediate graft are

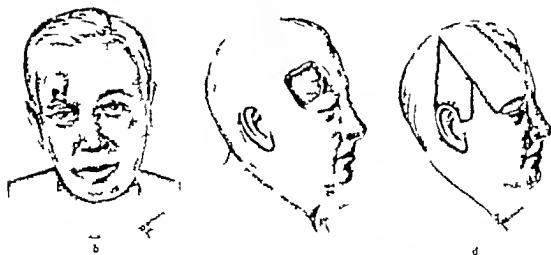


Fig. 4. Case 4. a, Basal cell carcinoma. b, had recurrent 3 times and had invaded the frontal bone and upper eyelid. c, Outline of radical excision. d, Diagram of defect after excision of tumor skin, frontal bone and upper eyelid. In one block had been made. e, Technique of forward

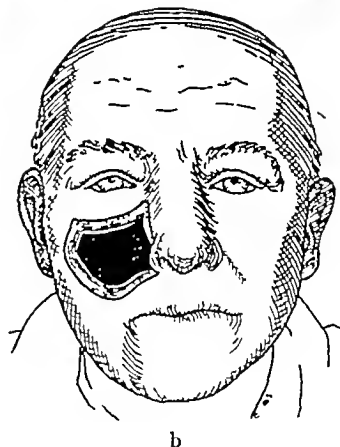
rotation of scalp flap. f, Parietal region of skull and upper eyelid were surfaced with thick split grafts. g, Postoperative appearance of patient. h, recurrence of carcinoma 4 years after operation. Patient refused further reparative surgery.

thicker than the Thiensch the intermediate embodying 75 to 90 per cent of the thickness of the skin. Although some plastic surgeons use the intermediate graft for facial reconstruction because of its ready availability the whole thickness graft is preferred at the New York Hospital because of the superior cosmetic result achieved by its use. The whole

thickness graft, as implied by its name embodies all of the layers of the skin and is cut according to pattern of the defect. The use of this graft leaves little to be desired since it provides an accurate match to the adjacent skin of the face in color texture moisture and movability on the underlying tissues. The upper eyelid, from which a graft 3 by 1.5



Fig 5 Case 5 a, Fibrosarcoma of cheek invading the maxilla b, Diagrammatic representation of the defect after radical excision of tumor together with anterior wall of maxillary sinus and hard palate c, Tubed temporal flap sutured into the maxillary defect The medial portion of this flap had been converted into a double faced flap by burying a thick split graft under it at an earlier operation d, Appearance after division of the pedicle and resuture of its base into the temporal region No recurrence 3 years and 2 months later



centimeters in size can be cut without producing deformity, and the postauricular area, which may yield a graft of 5 by 3.5 centimeters, are ideal sources for such grafts. If a large graft is required a donor area on the abdomen is necessary but it must be selected with due consideration for the growth of hair.

Case 2 demonstrates the successful result obtained with the use of a free, whole thickness skin graft to surface the defect produced by the excision of a malignant tumor of the skin.

Case 2 V L, New York Hospital No 60215, a 50 year old woman, was presented for treatment of a basal cell carcinoma of the skin of the right side of the nose which was three times recurrent following x ray therapy. At operation on September 29, 1937, this recurrent basal cell carcinoma was removed by excision as shown in Figure 2. All soft tissues were removed down to the bone and cartilage. A patterned whole thickness graft, which was cut from the posterior triangle of the neck, was sutured into the defect. Follow-up examination 4 years after operation showed no recurrence.

Case 3 demonstrates the method of rotation of a skin flap to provide a lining of skin in the repair of a through-and-through defect of the soft parts of the nose. The danger of relying entirely on biopsy material for a final tumor diagnosis is dramatically emphasized.

Case 3 J K, New York Hospital No 94807, a 32 year old man, was subjected in 1935 to subtotal thyroidectomy. Microscopic examination of sections cut from the specimen showed this to be a papillary adenocarcinoma of the thyroid. Intensive radiation was given to the neck and chest. Apparently the disease was under arrest when in February 1940 he noticed the development of a nodule over the alar cartilage of the nose on the right side. X-ray therapy



Fig. 4. Case 4. a, Basal cell carcinoma, which had recurred 5 times and had invaded the frontal bone and upper eyelid. b, Outline of radical excision. Diagram of defect after excision of tumor, skin, frontal bone and upper eyelid in one block had been made. c, Technique of forward

rotation of scalp flap. Parietal region of skull and upper eyelid were surfaced with thick split grafts. Postoperative appearance of patient 5 years after operation. No recurrence of carcinoma. Patient refused further reparative surgery.

thicker than the Thiersch, the intermediate embodying 75 to 90 per cent of the thickness of the skin. Although some plastic surgeons use the intermediate graft for facial reconstruction because of its ready availability, the whole thickness graft is preferred at the New York Hospital because of the superior cosmetic result achieved by its use. The whole

thickness graft as implied by its name embodies all of the layers of the skin and is cut according to pattern of the defect. The use of this graft leaves little to be desired since it provides an accurate match to the adjacent skin of the face in color, texture, moisture and movability on the underlying tissues. The upper eyelid, from which a graft 3 by 1.5

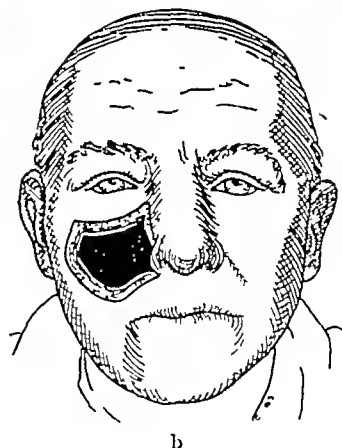


Fig 5 Case 5 a, Fibrosarcoma of cheek invading the maxilla b, Diagrammatic representation of the defect after radical excision of tumor together with anterior wall of maxillary sinus and hard palate c, Tubed temporal flap sutured into the maxillary defect The medial portion of this flap had been converted into a double faced flap by burying a thick split graft under it at an earlier operation d, Appearance after division of the pedicle and resuture of its base into the temporal region No recurrence 3 years and 2 months later

centimeters in size can be cut without producing deformity, and the postauricular area, which may yield a graft of 5 by 3.5 centimeters, are ideal sources for such grafts. If a large graft is required a donor area on the abdomen is necessary but it must be selected with due consideration for the growth of hair.

Case 2 demonstrates the successful result obtained with the use of a free, whole thickness skin graft to surface the defect produced by the excision of a malignant tumor of the skin.

Case 2 V L, New York Hospital No 60215, a 50 year old woman, was presented for treatment of a basal cell carcinoma of the skin of the right side of the nose which was three times recurrent following x ray therapy. At operation on September 29, 1937, this recurrent basal cell carcinoma was removed by excision as shown in Figure 2. All soft tissues were removed down to the bone and cartilage. A patterned whole thickness graft, which was cut from the posterior triangle of the neck, was sutured into the defect. Follow up examination 4 years after operation showed no recurrence.



Case 3 demonstrates the method of rotation of a skin flap to provide a lining of skin in the repair of a through-and-through defect of the soft parts of the nose. The danger of relying entirely on biopsy material for a final tumor diagnosis is dramatically emphasized.

Case 3 J K, New York Hospital No 94807, a 32 year old man, was subjected in 1935 to subtotal thyroidectomy. Microscopic examination of sections cut from the specimen showed this to be a papillary adenocarcinoma of the thyroid. Intensive radiation was given to the neck and chest. Apparently the disease was under arrest when in February 1940 he noticed the development of a nodule over the alar cartilage of the nose on the right side. X-ray therapy



Fig. 6. Case 6. a, Recurrent epidermoid carcinoma of eyelid with extension to the globe. b, Deformity after enucleation. The sacrifice of both eyelids. The cavity has been surfaced by application of thick split graft. c, Ap-

pearance of patient after fitting with glass eye attached to later prosthesis. 1 year and 4 months after operation.

failed to retard the growth of this lesion. The biopsy report was "apocrine adenoma or benign sweat gland adenoma. Because the appearance of the lesion suggested the invasive tendency of this tumor, radical excision was done September 28, 1950. The entire thickness of the wall of the nose including skin, cartilage and mucous membrane was removed as shown in Figure 3. The technical problem in this case was to provide a method of repair which afforded skin to line the nasal cavity and also to surface the wound. This could have been done by the use of a double faced flap from the cheek had such flap been prepared earlier. The technique of rotation of a flap downward from the upper portion of the nose to form lining and of surfacing the area with a whole thickness graft taken from the retroauricular area is demonstrated in Figure 3. With the entire tumor to his disposal, examination of the pathologist was able to ascertain that it was metastatic carcinoma of the thyroid. The graft healed nicely with good cosmetic effect. Multiple pulmonary metastases developed subsequently. At the present time the patient is still receiving x-ray treatments to the lung fields.

Cases 4, 5 and 6 are examples of the surgical management of advanced malignancy affecting the eye and the bones of the face. Radical surgical excision in cases of this type calls for boldness and courage since excision of any of the facial bones produces deformity which in itself may constitute cause for complete disability. It is in the management of these patients that a knowledge of reparative techniques and of the applications of prosthe-

ses offers the prospect of cure with rehabilitation. Although in theory prostheses represent the final failure of plastic surgery, their use has served to rehabilitate many unfortunate individuals and to contribute greatly to their happiness.

Case 4. D. W., New York Hospital No. 4, 403, 5 years old man, in 1933 presented himself for treatment of basal cell carcinoma of the forehead invading the frontal bone. Over period of 4 years this lesion had recurred 3 times following x-ray and radium therapy. Examination at the New York Hospital in 1933 disclosed the ulcerated lesion of the right forehead as shown in Figure 4. The growth had invaded the frontal bone, had destroyed the eyebrows, had produced some weakness of the superior rectus muscle. Vision in both eyes was good. There was extensive scar above the ulcerated area. Excision of the tumor in this case was done by Dr. George Heuer. The entire mass including the skin, the muscles of the upper eyelid, the frontal bone, and some of the frontal arched bone of the orbit was removed in one block. The frontal sinus was opened in the course of the resection. The dura mater appeared normal. Closure of the defect in the forehead was accomplished by the rotation of a flap hinged to the median sagittal line of the scalp. A thick split graft taken from the right thigh was used to cover the raw area on the parietal region of the skull produced by the forward rotation of the flap. A second smaller thick split graft was used to surface the right eyelid. The growth of hair in the right forehead region was arrested by means of x-ray treatment. The patient has now survived 8 years since

operation was performed. There is no local recurrence and he is in excellent general health. The appearance of the concave frontal area and the ptosis of the right eyelid have not bothered the patient sufficiently to convince him that it would be worth while to undergo further operation for cosmetic improvement.

Case 5 E. W., New York Hospital No. 192441, a 59 year old man, was examined at the New York Hospital for the first time in January 1938 because of a swelling of the right cheek and obstruction of the nasal passages on the right. Antiluetic and x-ray therapy had been administered without change in the size of the lesion. Examination showed a firm mass measuring 6 by 6 centimeters over the right maxilla. The mass was adherent to the skin and to the underlying maxilla. The nose was partially distorted as shown in Figure 5. Biopsy showed that the tumor was a retothelial (reticulocell) tumor of the face involving skin, subcutaneous tissue, and bone. On August 30, 1938, radical resection of the maxilla was done by Dr. William F. MacFee according to the technique described elsewhere by him. It was possible to save the bony floor of the orbit, the posterior wall of the maxillary sinus, the soft palate and the right upper lip. The hard palate was removed. Mucous membrane was sutured to skin wherever possible. The patient made an uneventful recovery. On March 16, 1940, approximately 7 months after resection of the maxilla a temporal flap was fashioned at operation and sutured down in place as shown in Figure 5. Division of the flap at its medial end was done on March 25, 1940. On April 10, 1940 the flap was re-elevated and two thick split grafts were taken from the thigh and buried face to face under the upper and medial end of the flap. This served to make the flap a double faced one in its distal portion. When the flap was elevated again at operation on May 6, 1940 the donor area over the frontal bone was found to be neatly surfaced by the thick split graft which had been placed at the previous operation. The pedicle was tubed by suture and its distal, double faced end was transplanted to the maxillary region as shown in Figure 5. In the final operative procedure the pedicle was detached and its base was replaced in its normal position in the preauricular and temporal regions. The patient has been equipped by Dr. Harold Genvert of this clinic with a nicely fitted upper dental plate which carries an obturator to fit into and fill the defect in the hard palate. Follow up examination 3 years and 2 months after excision of the tumor showed the patient to be in excellent general condition with no evidence of recurrence or metastasis.

Case 6 I. M., New York Hospital No. 237954, a 64 year old woman, had a tumor of the lower eyelid removed by her physician by cautery in 1936 and again in 1938. Examination in July, 1939, showed an adherent ulcerated tumor of the skin near the inner canthus of the right eyelid. The tumor involved nearly half of the upper and lower lids. There was congestion of the conjunctiva and the tumor could

be seen growing out onto the cornea. There was dimness of vision but not complete loss of sight. There was no cervical adenopathy. Enucleation was necessary to effect cure. The appearance of the lesion is shown in Figure 6. At operation on July 19, 1939 the eyeball together with both eyelids and all orbital structures was removed. Microscopy showed the tumor to be an epidermoid carcinoma. A thick split graft was applied to the wound after wrapping it about a mass of dental stent, previously molded to fit the cavity. The orbital bones were exposed in the floor of and on the medial aspects of the wound. It was not possible to preserve enough of the lower eyelid to help in the application of a prosthesis. The patient was fitted with a glass eye which is held in the socket by means of a latex prosthesis (6). This patient reports every 3 months for inspection of the grafted area. At these visits the prosthesis is retinted, replaced and held by means of liquid adhesive. There has been no recurrence to the present date, 2 years and 4 months after operation.

SUMMARY AND CONCLUSIONS

In this report an analysis is made of 100 cases of malignancy of the face treated by surgery over an 8 year period. There were 55 cases of basal cell carcinoma of which 15, or 27 per cent, were recurrent tumors when presented for surgical treatment. There were 21 cases of epidermoid carcinoma of which 9, or 43 per cent, were recurrent tumors. Study of these records shows that in the majority of the recurrent tumors, primary treatment had been inadequate. This analysis of data serves to emphasize the responsibility of the doctor to provide adequate curative primary treatment for malignant lesions of the face. In 7 cases of the 100 in the series, the tumor had invaded the bones of the face. The indications for the use of grafts, flaps, and prostheses are demonstrated by means of 6 detailed case reports. If utilized by surgeons, the principles of reparative surgery serve to assign a high percentage of malignant tumors of the face to treatment by radical surgical excision.

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THE USE OF VERMILION BORDERED FLAPS IN SURGERY ABOUT THE MOUTH

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VERMILION bordered flaps have proved one of the most effective methods of correcting defects or deformities about the mouth. Although American authors commonly attribute the operation to Abbe the method was first described by Estlander in 1872 26 years before Abbe a paper appeared

Estlander's paper was published in Swedish in the *Nordiskt medicinskt Arkiv* under the title "A Method of Replacing Lost Tissue in one Lip and Cheek from the Other Lip." A similar report from him appeared that same year in the *Archiv für klinische Chirurgie* (6). A later description of his method was published in French in 1877 (7). It is much the same as that of the original paper.

Estlander had observed that after wide excision of the lower lip for malignant disease closure was possible only with tension on the skin margins and a great difference in the width of the lips. He decried the tendency among surgeons, when confronted with a large

defect in the lip to search out and utilize remote tissues from the cheeks or neck, neglecting entirely the most available tissue—namely the other lip. While studying the anatomical relationships of the vessels about the mouth he realized that large flaps could be nourished by the encircling coronary artery alone. He determined and described accurately the relation of this vessel to the skin and mucosa of the lip and indicated the importance of this relation in avoiding injury to the vessel while preparing the flap and turning it on its narrow pedicle. Several case histories and complete descriptions of the operations are presented to indicate where and how the procedure is applicable. There are illustrative drawings of one of these cases showing how by use of this method the defect from excision of half of the lower lip for carcinoma was repaired by switching a flap from the upper lip. A new corner of the mouth was formed by the pedicle. In another case there was loss of one ala of the nose part of the upper lip and the adjacent cheek as a result of a noma. Estlander illustrates its correction with a large vermilion bordered flap turned up from the lower lip. One margin of the flap was cut across and adjusted to form

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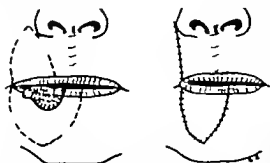


Fig. 1. Illustrating the use of a vermilion bordered flap in the primary repair of a defect from wide excision of the lower lip, adjacent to the corner of the mouth. a, Left, dotted lines indicate the area excised from lower lip and outline of flap of the upper lip. b, The completed repair.



Fig. 2. A patient in whom excision and repair were carried out by method here illustrated in Figure 1. The narrow pedicle on which the flap is carried, can be seen.

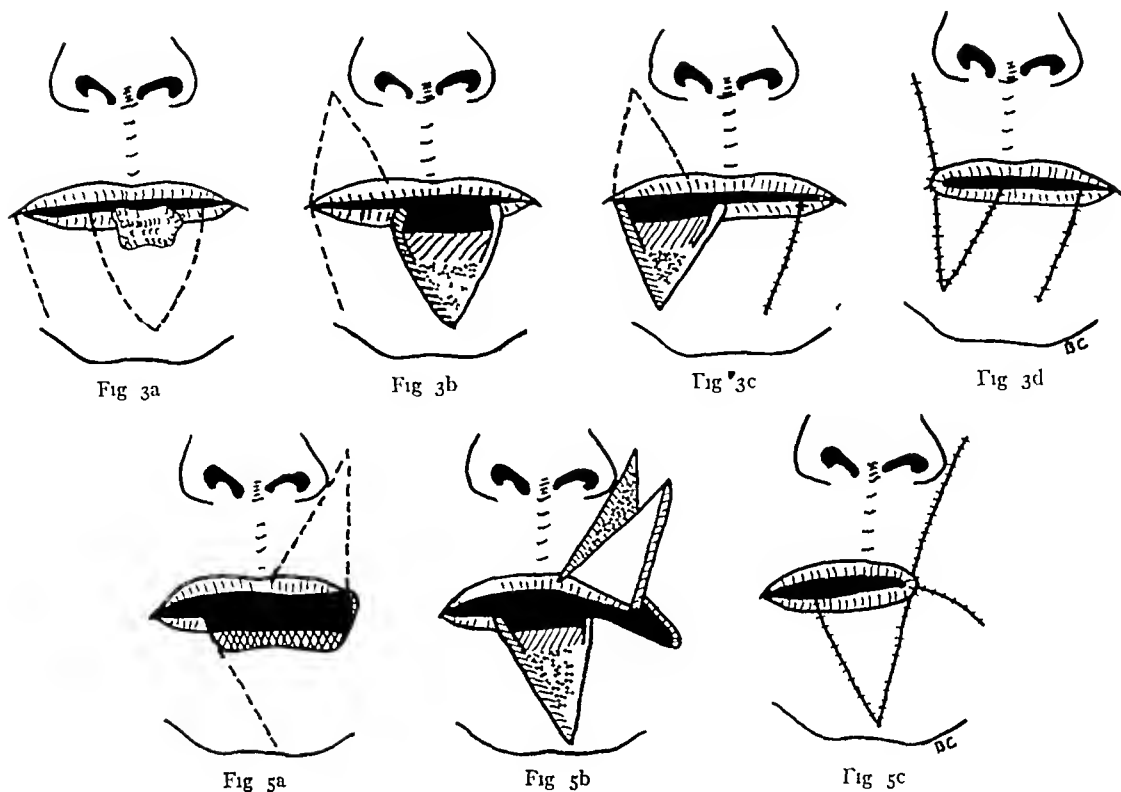


Fig 4



Fig 6

Fig 3 Illustrating the use of a vermilion bordered flap in the primary repair of a defect from a wide excision of the center of the lower lip. A quadrangular flap is shifted into the midline defect and the repair is completed by means of dotted lines. In b, The dotted lines indicate the area excised from the lower lip and the outline of the quadrangular and triangular flaps, c and d, the shifting of the flap and the completed repair.

Fig 4 A patient in whom excision and repair were carried out by method shown in Figure 3

Fig 5 Illustrating the use of a vermilion bordered flap in the repair of a pre existing defect in the lower lip. a, The defect is outlined and the incisions are indicated by means of dotted lines. In b the shifting of a local triangular flap in the lower lip and a vermilion bordered flap from the upper is illustrated. In diagram c the completed repair is shown.

Fig 6 A patient in whom surgical repair was carried out by method which is shown in the diagrams of Figure 5

the ala, the remainder fitted to the lip and cheek. In this case also a corner of the mouth was formed by the pedicle.

Abbe's paper in 1898 was the first description of the operation in English, and the first

in which the pedicle crossed the mouth and was later severed. He reported a single case and only briefly outlined and illustrated the method. His contribution should be considered a modification of the original method.

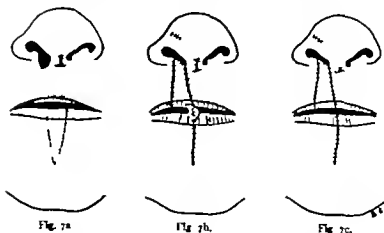


Fig. 7a

Fig. 7b.

Fig. 7c.



Fig. 8.

Fig. 7. Illustrating the use of vermillion bordered flap in secondary correction of unilateral harelip deformity. a, Showing the tight retracted upper lip and deficient floor of the nose. The outline of the flap is indicated by dotted lines. b, The flap is in place in the upper lip with the

pedicle crossing the mouth. c, The completed repair showing relaxation of the upper lip and correction of the floor of the nose.

Fig. 8. A patient in whom secondary correction was carried out by method shown in Figure 7.

and full credit is due Estlander for the introduction of his fundamental concept many years before.

The indications for the use of vermillion bordered lip flaps have been demonstrated and extended by surgeons in recent years (2, 3, 8, 9) and there have been modifications of the flap itself (4) but the primary principle which consists of carrying a large direct vermillion bordered flap on a narrow pedicle with a single nutrient artery has remained unchanged.

The simplest use of the flap is one in which there is a defect in the lower lip adjacent to the corner of the mouth, too large for primary closure. This method is similar to that used by Estlander in one of his illustrative cases (Figs. 1 and 2).

CASE. C. P. H. 40-73. A male 57 years of age had a large irregular ulcerated lesion of the right lower lip 1.5 centimeters in diameter which extended deeply into the substance of the lip and which proved to be squamous cell carcinoma, grade II. The operation was done under local anesthetic. The two mental nerves, the right infraorbital, and the few cervical branches that reached upward to the chin were blocked with per cent novocain. Nerve block is preferable to local infiltration because infiltration may jeopardize the blood supply to the flap by local trauma and tension within the tissues. A wide V-excision of the diseased area was then carried out. This involved removal of over half the lower lip from the corner of the mouth to beyond the midline on the opposite side and down to the alveolus. A large triangular flap, half the width of the defect, was then raised from the upper lip and cheek in the nasolabial fold and turned downward into its new position. The pedicle of the flap containing the coronary artery formed the new corner of the mouth. It was carefully sutured into place with

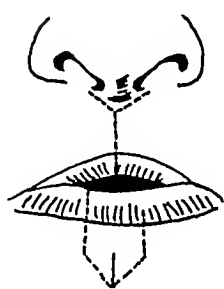


Fig 9a

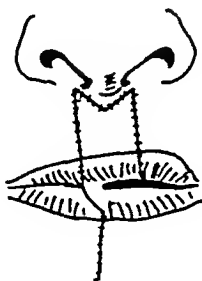


Fig 9b

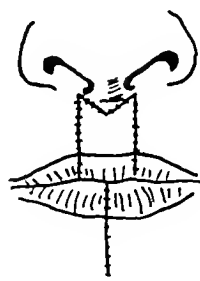


Fig 9c



Fig 10

Fig 9 Illustrating the use of a split vermilion bordered flap in the secondary correction of a double harelip deformity a, The dotted lines indicate the outlines of the flap and the incision in the upper lip b, The flap is in

place in the upper lip with the pedicle crossing the mouth c, The completed repair

Fig 10 A patient in whom the prolabium was excised and replaced with a split vermilion bordered flap

deep vertical mattress sutures in the mouth and fine interrupted silk sutures in the skin. A right suprahyoid dissection was done 6 months later because of a palpable node but no metastases were found. There has been no recurrence after a full year.

This patient, before operation, was fearful that extensive relaxing incisions would be necessary in the cheek and that he might lose his job because of his appearance. The functional and cosmetic results, however, by this method, are very satisfactory to the patient.

A second method is used when the neoplasm involves the center of the lower lip. If the defect is so large that it cannot be closed primarily, a quadrangular flap extending to the corner of the mouth is shifted into the defect and the repair is completed in a similar manner to that of the first method (Figs 3 and 4).

CASE 2 C P H 22-1144 A man 56 years of age, had a large, round, ulcerated lesion of the

middle of the lower lip 2 centimeters in diameter which proved to be squamous cell carcinoma, grade I. At operation, also with local nerve block anesthesia, a wide V excision of the diseased area was carried out. This involved the removal of over one-half the center of the lower lip. A quadrangular flap of normal lip was shifted across the midline to the left, and the remaining defect was closed with a triangular vermilion bordered flap turned down from the upper lip. Neck dissection has not been done but the patient is under careful observation.

A third method is useful when there is a pre-existing defect from surgical excision of the lip for carcinoma or for other causes. A triangular or rectangular flap from the upper lip is turned into the defect in the lower and the adjacent tissues adjusted to it (Figs 5 and 6).

CASE 3 P M H 40-1003 A man, 76 years of age, had a squamous cell carcinoma, grade III of the lower lip with metastases to the neck. The excision of the lesion of the lip and a left radical neck dissection were done by Dr C C Franseen. At operation,

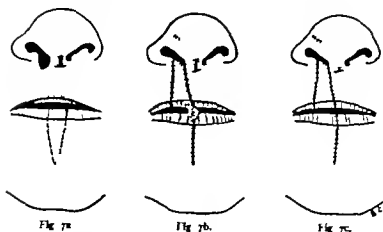


Fig. 8.

Fig. 7. Illustrating the use of vermillion bordered flap in secondary correction of unilateral harelip deformity. a, Showing the tight retracted upper lip and deficient floor of the nose. The outline of the flap is indicated by dotted lines. b, The flap is in place in the upper lip. c, With the

pedicle crossing the mouth. c, The completed repair showing relaxation of the upper lip and correction of the floor of the nose.

Fig. 8. A patient's lower secondary correction as carried out by method shown in Figure 7.

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The indications for the use of vermillion bordered lip flaps have been demonstrated and extended by surgeons in recent years (2, 3, 8, 9) and there have been modifications of the flap itself (4) but the primary principle which consists of carrying a large direct vermillion bordered flap on a narrow pedicle with a single nutrient artery has remained unchanged.

The simplest use of the flap is one in which there is a defect in the lower lip adjacent to the corner of the mouth, too large for primary closure. This method is similar to that used by Eastlander in one of his illustrative cases (Figs. 1 and 2).

CASE 1. C. P. H. 40-73. A man, 37 years of age, had a large irregular ulcerated lesion of the right lower lip, 3 centimeters in diameter which extended deeply into the substance of the lip and which proved to be squamous cell carcinoma, grade II. The operation was done under a local anesthetic. The trigeminal nerves the right infraorbital, and the few cervical branches that reached upward to the chin were blocked with 1 per cent novocain. Nerve block is preferable to local infiltration because infiltration may jeopardize the blood supply to the flap by local trauma and tension within the tissues. A wide V-excision of the diseased area was then carried out. This involved removal of over half the lower lip, from the corner of the mouth to beyond the midline on the opposite side and down to the bucculae. A large triangular flap, half the width of the defect, was then raised from the upper lip and cheek, over the nasolabial fold and turned downward into its new position. The pedicle of the flap containing the coronary artery formed the new corner of the mouth. It was carefully sutured in place with

HYPOPROTHROMBINEMIA AND LIVER FUNCTION

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PLASMA prothrombin and methods for measuring this clotting factor have attracted much interest in recent years. Even before the need for vitamin K was known, it had been shown (18, 22) that intact liver function is necessary for the production of prothrombin. With the widespread clinical use of vitamin K, it soon became apparent that liver disease interferes with the prothrombin response to vitamin K therapy in human patients (4, 5, 6, 13, 16, 19, 20). Additional studies with liver extirpation confirmed the vital rôle of the liver in prothrombin production (1, 20, 23). Hypoprothrombinemia, thus, may result either from a deficiency in vitamin K, or from liver disease. This necessity of a good state of liver function to maintain normal prothrombin production naturally has suggested the possible use of the prothrombin level as a measure of liver function. Wilson (24, 25) studied the correlation of the prothrombin level and the hippuric acid liver function test and concluded that these two usually gave parallel results and reflected the state of the liver much better than did other liver function tests. More recently Lord and Andrus (8) and Olwin (11) have stressed the value of the prothrombin level and the response to vitamin K in the differential diagnosis of intrahepatic and extrahepatic jaundice. On the other hand, Lucia and Aggeler (10) found little correlation between the hippuric acid liver function test and the prothrombin level. Lucia and Aggeler used the prothrombin method of Quick (14, 15) whereas the others used the two stage method of Warner, Brinkhous and Smith (18, 22). It appears probable that differences in the prothrombin methods employed are responsible for the differences in the results obtained by these workers.

We wish to present studies correlating the plasma prothrombin level with other evidence of liver disease, and, particularly, to compare the results obtained with different prothrombin methods. The data obtained so far indicate that in human patients hypoprothrombinemia which does not respond to vitamin K therapy is a reliable index of liver disease and that prothrombin techniques differ in sensitivity in this respect.

Before presenting the cases studied, we wish to give a brief résumé of the prothrombin methods available. The several prothrombin methods in current use in this country fall into two groups and can be classified as one stage and two stage methods. In the two-stage procedure, developed by Warner, Brinkhous, and Smith (18, 22), the prothrombin of plasma is converted into active thrombin as a preliminary step. In a second step, the thrombin thus produced is measured by determining the speed with which it will clot a standard fibrinogen solution. In contrast, the one stage methods simply measure the clotting time of blood or plasma in the presence of excess thromboplastin. These latter methods, thus, are dependent upon a summation of the time required for the thrombin to act in clotting. They serve as a very practical index of the capacity of the blood to clot and, thus, of the tendency of the patient to bleed. The method of Quick (14, 15) and the more simple "bedside" test (27) developed in our laboratory, which gives essentially the same results as the Quick's method, are of this type. Also several modifications (3, 7, 26) of these are in this category.

All of the methods in current use give satisfactory results for the clinical control of vitamin K therapy, and all serve to detect the hypoprothrombinemia which results from acute severe liver injury. However, with milder degrees of hypoprothrombinemia, particularly if of a chronic nature, it appears that an altered convertibility of prothrombin

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8 months later a triangular vermilion bordered flap was raised from the left upper lip. There was no hazard in using this flap because although the left facial artery had been severed during the neck dissection that on the right which is the side from which the flap is nourished, was intact. By extending an incision obliquely downward from the right border of the defect of the lower lip triangular space was created into which the flap was fitted. The second flap, thus formed from the lower lip, as shifted to the newly created corner of the mouth on the left and adjusted to the adjacent cheek.

A fourth method similar to that described by Abbe is useful in the secondary correction of unilateral harelip deformities. The tight upper lip and the often deficient floor of the nose can be improved by utilizing a flap from the lower lip giving a more pleasing relationship between the two. By this method both the fullness of the lower lip is reduced and tissue is added to the upper lip. The pedicle which must cross the mouth is severed after 2 to 3 weeks (Figs. 7 and 8).

CASE 4. M. G. H. 126720. Patient is girl, 5 years of age. The primary repair of the lip, done in childhood, left her with tense retracted upper lip, deficient floor of the nose and unsatisfactory suture marks on both cheeks. At operation, under tracheal ether anesthesia, the difference in width between the two lips was determined and a vermilion bordered flap half this width was prepared in the midline of the lower lip. The old scar in the upper lip was opened and extended into the floor of the nose. The flap was turned into this defect the vermilion borders were accurately proportioned, and the tip of the flap was fitted into the floor of the nose. Two weeks later the pedicle of the flap was severed and the mucosal edges were closed. Most of the operative procedure was carried out by D. S. H. Sturge.

A fifth method is useful for secondary corrections following harelip repair when there is nasal symmetry. The lip is opened in the midline with extensions across the base of the columella into the floor of each nostril. A split vermilion bordered flap is used. The splitting of the flap leaves a better balanced lip with scars that are not apparent (Figs. 9 and 10).

CASE 5. M. G. H. 59,700. Patient of D. S. H. Sturge. A girl, 3 years of age had partial double harelip repaired in childhood. In the initial repair the proboscis was utilized to form the vermilion border in the midline. Because of the notching of the upper lip and because of the deficiency of tissue

bulk in the proboscis, a split vermilion bordered flap from the lower lip was used. At operation, under general anesthesia instead of opening the lip in the midline as indicated in the diagram, the proboscis was completely excised in this case and replaced by the flap.

When the pedicle of the flap forms a new corner of the mouth, as in the first 3 cases, it can later be severed just as is the pedicle that crosses the mouth. In this way the width of the opening is increased and the patient can use the mouth more comfortably. It is important, however, not to extend the incision laterally beyond the pedicle of the flap as the patient may then have difficulty in controlling the corner of the mouth and in preventing the leakage of saliva. After the patient has become accustomed to the altered condition of the mouth there is seldom much difficulty with function for sufficient residual muscular action remains to control the motions of the mouth. The scars of the face and lips resulting from the procedure are not disfiguring because they lie in the nasolabial fold and vertically on the lip. Little distortion of the mouth is caused by the scars either at rest or while the mouth is in motion.

SUMMARY

The vermilion bordered lip flap was first described by Eastlander in 1872. It is useful in repairing the lip after a wide excision for carcinoma, as the need of widespread relaxing incisions in the cheek is eliminated and no normal tissue is sacrificed. It is also useful for the secondary correction of harelip deformities both in securing a better balance between the upper and lower lips and in replacing deficiencies in the floor of the nose. Five cases in which the flap was used are presented.

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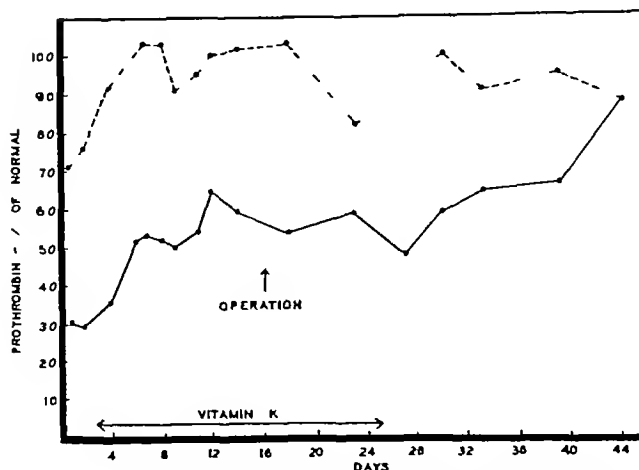


Fig 4 Prothrombin response to vitamin K therapy Central liver necrosis - · - ·, Bedside technique, —○—, two stage technique

The amount of prothrombin, as indicated by the two stage method, was greatly reduced. The clotting power of the blood, however, as indicated by the one stage method was only moderately impaired. As would be expected in cases in which the lowered prothrombin was due primarily to liver disease, vitamin K did not correct the hypoprothrombinemia. A poor and incomplete response was indicated by the one stage test, but no response was demonstrable by the two stage test. The patient came to autopsy and an extreme degree of cirrhosis of the liver (Fig 2) was found. This marked liver damage, indicated by the ineffectiveness of vitamin K, was mainly responsible for the hypoprothrombinemia.

Figure 1, C, represents a case of Banti's syndrome. Here again, the hypoprothrombinemia was associated with extensive liver damage and the administration of vitamin K was ineffective. As in the preceding case, the two stage prothrombin method proved to be a more sensitive index of the liver damage than did the one stage test. The hypoprothrombinemia, as indicated by the two stage method, was much more severe than was apparent from the one stage test. Also, the ineffectiveness of vitamin K was more evident by the two stage method. We have noted that there is usually some shortening of the one stage clotting time following vitamin K therapy, irrespective of the type case with which we

are dealing. The biological significance of this fact is not yet apparent. This patient died following splenectomy and the liver (Fig 3) showed extensive cirrhosis.

Figure 4 represents a case of hepatitis with jaundice. In this case the prothrombin level showed some response to vitamin K by both methods, indicating, we feel, that there was some deficiency of this vitamin. The main cause for the lowered prothrombin, as well as of the jaundice, however, was the liver damage, and the more sensitive two stage prothrombin method indicated a very incomplete response. This patient was explored and the

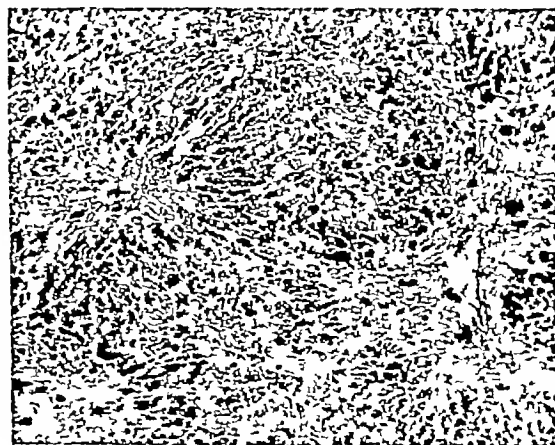


Fig 5 Microscopic section of liver in case of severe hepatitis with jaundice

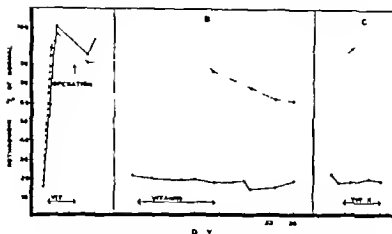


Fig. 1. Prothrombin response to vitamin K therapy. A, Stricture of bile duct. B, portal cirrhosis. C, Bant's disease. —○— Two stage technique.

may compensate for a considerable decrease in the actual amount of prothrombin present (13-28). In instances of this type, the two stage method appears to be a much more sensitive index of the true prothrombin level than are the one stage methods and, therefore is a better index of liver function.

Figure 1 A, represents a case in which an obstruction of the common bile duct resulted in vitamin K deficiency. The hypoprothrombinemia, shown by both the two stage and the one stage methods responded promptly and completely to the administration of the vita-

min. In this case by all available criteria, the functional capacity of the liver was within normal limits and the lowered prothrombin was due entirely to a vitamin K deficiency.¹ This case illustrates the normal response to vitamin K therapy.

Figure 1 B represents a case of portal cirrhosis of the liver. Bile was present in the bowel, and there was no reason to suspect that the vitamin K intake was inadequate.

¹It is believed that for the purpose of standardizing responses with the prothrombin test, the best way to administer the vitamin is by the intravenous injection of one of the synthetic water soluble preparations.

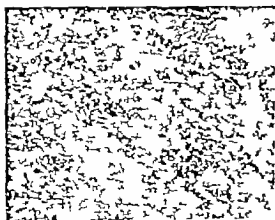


Fig. 2. Microscopic section of liver from case of extrahepatic cirrhosis of bile duct which did not respond to vitamin K therapy.



Fig. 3. Microscopic section of liver showing extrahepatic cirrhosis, from case of Bant's disease which did not respond to vitamin K therapy.

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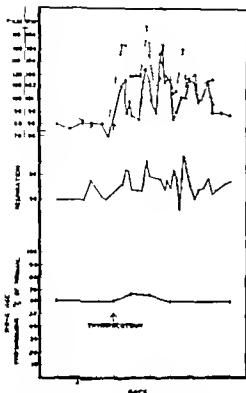


Fig. 6. Prothrombin level temperature — pulse, and respiration in case of thyroid crisis with recovery

extrahepatic biliary tract was found to be entirely normal. The very gradual return of the prothrombin level to normal coincided with clinical recovery of the patient. A biopsy of the liver at the time of exploration showed extensive liver necrosis (Fig. 5). This case is one in which the extensive liver damage, indicated by the two stage method, strongly suggested that the jaundice was of intrahepatic origin before exploration, and illustrates the usefulness of prothrombin studies in differential diagnosis as well as in prognosis.

During the past few years, increased emphasis has been placed on changes occurring in the liver associated with hyperthyroidism, (2, 9, 17). Figure 6 represents a case of thyroid crisis with recovery. The preoperative and postoperative prothrombin levels were moderately reduced indicating moderate impairment of liver function in this case. Still more striking is a recent fatal case of post-

operative thyroid crisis. In this patient the prothrombin level as determined by the two stage method fell to 16 per cent of normal. Vitamin K therapy was instituted, but the patient died before a second prothrombin determination could be made. Extensive hemorrhage, no doubt due to the lowered prothrombin, was at least a contributing factor in the fatal outcome. These 2 cases, of course, are not sufficient to justify ultimate conclusions, but they are in accord with the thesis that hepatic insufficiency is an important factor in fatal thyroid crisis.

In all of the cases we have studied the two stage procedure has appeared to be a more sensitive index of liver damage than have the one stage tests. If further work establishes prothrombin determinations as a useful index of liver function it may be that some simplification of the two stage test can be developed which will render it more suitable for general use.

SUMMARY

From our results, as well as from reports in the literature it appears that determination of the prothrombin level has considerable promise as an index of liver function. Hypoprothrombinemia due to a vitamin K deficiency responds rapidly to specific therapy. Failure to obtain this response appears to indicate liver disease.

Unfortunately it appears from the work to date that the simple one stage tests, which have proved so satisfactory for the control of vitamin K therapy, are not nearly as sensitive an index of liver damage as is the more complicated two stage method. The latter method could probably be simplified.

Preliminary studies of prothrombin levels in thyroid crisis lend some support to the thesis that the liver is concerned in this condition.

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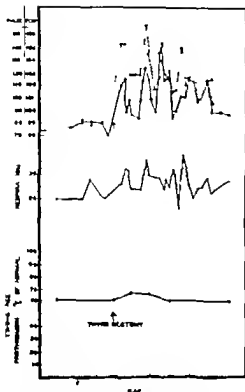


Fig 6. Prothrombin level, temperature, pulse, and respiration in case of thyroid crisis with recovery.

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In all of the cases we have studied the two stage procedure has appeared to be a more sensitive index of liver damage than have the one stage tests. If further work establishes prothrombin determinations as a useful index of liver function. It may be that some simplification of the two stage test can be developed which will render it more suitable for general use.

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THE HEALING OF ANASTOMOTIC WOUNDS IN ASEPTIC GASTRIC SURGERY

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THE object of this paper is to report some of the work done in the experimental laboratory during the development of a technique for aseptic gastric surgery. During the past 2 years all gastric operations on the surgical clinic service at the Stanford University Hospitals have been done with a closed or aseptic procedure. The technique of this operation and the clinical experiences with its use have been reported by Dr. Emile Holman. In the early stages of the conversion from open anastomosis to an aseptic technique certain questions arose relative to the use of clamps, methods of suturing and the healing of wounds made with the cautery.

Although aseptic anastomosis in the intestine has been practiced for many years the use of this principle in gastrointestinal surgery has found few advocates. Wangensteen (14) recently described a method of doing closed anastomoses adaptable to any segment of the alimentary canal and followed this publication with another (15) in which he described his experiences with the technique after using it in 100 consecutive cases. As Wangensteen indicated probably the following two factors more than any others, have deterred surgeons from using a closed anastomosis: namely danger from hemorrhage and fear of poor mucosal healing if the mucous membranes are not approximated.

Three choices are open to the surgeon in preventing bleeding in gastric surgery. The first is the clamping and ligating of the individual gastric vessels, which method is tedious and necessarily involves spilling some blood and gastric content into the operative field. The second is the use of a continuous hemostatic suture as an inner layer which

must be placed tightly enough to constrict the vessels. Such constriction is injurious to the tissues. Healing with this type of suture has been found to be poor and is attended by considerable edema and infection (9). The third method is the use of the cautery to seal the wall sufficiently to coagulate the vessels.

Few studies have been reported on the healing of gastrointestinal wounds made with the cautery. Klose and Rosenbaum-Canné believed that section by cautery produced more inflammation and delayed union than did division with knife. Their observations were made on 16 cats in which simple incisions were made through the wall of the stomach, these wounds being closed with various methods of suturing. Kopyloff studied the comparative healing of gastroenterostomies, the incisions being made with scissors, knife and cautery and sutured by different methods. His results led him to believe that cautery incisions caused pronounced inflammation and delayed healing. His work throws little light on the subject, however, since in the 8 animals in which cautery incision was done the specimens were removed between 25 and 180 days after operation. Only 1 early specimen was studied.

The healing of gastrointestinal wounds made with the scalpel or scissors, and the effect of using various suture materials and methods have been described amply by others. Martzloff and Suckow (9) in 1933 summarized the literature on wound healing in gastroenterostomy and reported observations on 44 dogs. They found that the most rapid healing was obtained by the use of a single layer of Halsted serosubmucosal protection sutures of silk. They were of the opinion that separate suture of the mucosa was unnecessary and actually retarded healing. Furthermore sutures placed to evert the mucosa often caused epithelium to develop in the line of gastrointestinal apposition, resulting in adenomatous

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structures Their findings indicate that healing takes place more rapidly when the mucosa is left unsutured

PLAN OF STUDY

Twenty-seven full grown dogs were used They were given only water for 24 hours preceding the operation One hour before operation, morphine sulphate, 2 grains, was given hypodermically Anesthesia was maintained with inhalation ether In 17 animals an aseptic anterior gastroenterostomy was done and in 10 animals aseptic gastric resection was performed The Waffler cautery was used to divide the stomach and intestine After operation the animals were fed water the first day, milk the second, milk and gruel the third and fourth, and from then on, the standard dog chow They were sacrificed with chloroform at from 1 to 3 day intervals from the 2d to 34th day Specimens were removed while the animals were living, and were fixed in formalin Segments were cut from the midportion of the anastomosis, embedded in paraffin, and the sections were stained with hematoxylin-eosin and van Gieson

OPERATIVE PROCEDURE

The procedure used in these experiments was the same in principle as the one reported by Emile Holman In the early experiments the gastric resections were done with the use of only Payr clamps at the line of transection, the suturing then being done over these same clamps In the more recent experiments, the Payr clamp was replaced, after the wall was crushed, by either a Martzloff or a Wangenstein clamp Another crushing clamp was applied distal to the anastomosis clamp and the intervening segment of stomach wall was divided with the Waffler cautery A 3 millimeter cuff of tissue was left protruding beyond the clamp and this cuff was then seared for 15 seconds with the cautery Reasons for leaving the cuff are given below The jejunal stoma was made by excising with the cautery a segment of the antimesenteric wall protruding beyond an anastomosis clamp, again allowing the seared cuff to project 3 millimeters beyond the clamp Preliminary crushing with a Payr clamp was not found to be

necessary in the jejunum In the simple gastroenterostomies the stomach opening likewise was made by excising a segment of the anterior gastric wall protruding beyond an applied anastomosis clamp, the same 3 millimeter cuff being left projecting beyond the clamp An assistant held the anastomosis clamps while the sutures were placed

The prevention of hemorrhage in closed anastomoses presented a problem which was solved after we had experimented with various means of treating the divided end of the stomach It was found that crushing alone did not prevent bleeding Furthermore, if one simply and rapidly cuts the stomach from the anastomosis clamp with the actual cautery, brisk hemorrhage may result when the clamps are withdrawn Heating the anastomosis clamp with the Waffler cautery for 20 to 30 seconds will insure coagulation of the vessels, but this method has the disadvantage of damaging the contiguous stomach wall by heat transmitted from the clamp The one fatality in the series occurred in an animal in which this method was used, death was due to localized peritonitis resulting from sutures giving way in an area damaged by transmitted heat When the electrocoagulating unit was applied to the anastomosis clamp, it was found that high voltage for a long period of time was necessary to prevent bleeding, producing the same injury as did heating the clamp with the actual cautery

These experiences led to the adoption of the method of leaving a 3 millimeter cuff of tissue protruding above the clamp when the stomach or intestine was resected When the cuff was seared with the actual cautery at bright red heat for 15 seconds most effective hemostasis resulted, and damage to the tissues beneath the clamp was prevented A study of early specimens showed that this cauterized cuff had disappeared almost entirely in 48 hours, probably from the action of the digestive juices In no instance did it lengthen the flange or cause obstruction The area crushed with the Payr clamp formed the granulating bed The large vessels which approached the line of anastomosis were underrun with a silk suture on an intestinal needle and then tied



Fig. 6 Twenty-one day healing, Dog 9, gastroenterostomy. a, line of apposition; b, healed serosal membrane with gland formation; c, intestine; d, stomach.

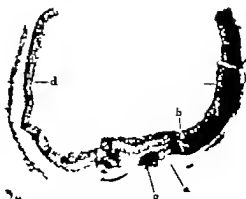


Fig. 7 Twenty-eight day healing, Dog 10, gastric resection. a, line of apposition; b, mucous membrane with glands; c, site of union; d, intestine; e, stomach; e, area of lymphoid hyperplasia. Not absence of flange.

stages of healing except near the base of the granulating bed. By the eleventh day the line of serosal union was replaced by a zone of fibrous tissue in which the frayed ends of the muscularis could be seen.

SIZE OF THE FLANGE

Beginning with the 14 day specimens there was a definite decrease in the height of the flange. By the 18th day it was considerably smaller and in twenty-eight days the site of union was represented only by an area of slight thickening. It would appear that irritation from a granulating bed has something to do with maintaining the flange for

as soon as it was covered with mucosa the flange regressed.

MICROSCOPIC DESCRIPTION OF REPRESENTATIVE SPECIMENS

Figure 1: 5 day—Dog 5—gastroenterostomy. The line of apposition showed minimal inflammatory response. A broad granulating bed, as present, covered by fibrinocellular membrane. The chronic suture was surrounded by collection of polymorphonuclear leukocytes. On the stomach side of the defect the epithelium had begun to grow out as single layer. On the intestinal side the epithelium also had begun to cover the ulcer but there was less growth than from the stomach side. The mucosa



Fig. 8 Thirty-two day healing, Dog 9, gastric resection. a, line of apposition; b, healed serosal membrane with glands; c, intestine; d, stomach.



Fig. 9 Sixty day healing, Dog 9, gastroenterostomy. High power photomicrograph showing single layer of epithelial cells growing from stomach side. a, granulating bed; b, fibrinocellular membrane; c, marginal cysts; d, early gland formation.

membrane adjacent to the defect showed some edema and cellular infiltration

Figure 2 9 days—Dog 22—gastroenterostomy The line of apposition was filled with a thin layer of fibrin in which there were only scattered leucocytes The granulating bed was about one-third the diameter of the 5 day specimen The epithelial growth on the stomach side showed early gland formation and 3 marginal cysts There was about an equal amount of epithelial regrowth and gland formation on the intestinal side

Figure 3 11 days—Dog 24—gastroenterostomy The line of apposition was practically obliterated by a fibrous tissue zone Some granular debris was present in this region On one side the epithelium had grown over the entire granulating bed, being joined in the center by a narrow area of single celled epithelium In another area the mucous membrane had not healed, the appearance being that of a 7 day specimen Well defined gland formation was present

Figure 4 14 days—Dog 2—gastric resection The line of apposition was replaced by fibrous tissue The mucous membrane lay in apposition There was definite gland formation, especially on the stomach side of the anastomosis The granulating bed was covered by a single layer of epithelium A silk suture in the muscularis was surrounded by a collection of polymorphonuclear cells The flange was smaller than the earlier specimens

Figure 5 18 days—Dog 5—gastric resection The line of apposition was demarcated by a zone of fibrous tissue in which the frayed ends of the muscle could be seen The mucous membrane was healed by a single layer of epithelium A silk suture surrounded by inflammatory cells lay near the healed mucous membrane The flange was barely present

Figure 6 21 days—Dog 11—gastroenterostomy The mucous membrane had healed completely with definite gland formation at the juncture A small flange was present

Figure 7 28 days—Dog 10—gastric resection The mucous membrane had healed completely with gland formation at the point of union An area of lymphoid hyperplasia was present in the muscularis of the stomach The flange was represented by an area of slight thickening

Figure 8 32 days—Dog 9—gastric resection The microscopic appearance was similar to the 28 day specimen

Figure 9 6 days—Dog 12—gastroenterostomy The gross and microscopic picture was about the same as the 5 day specimen A high power photomicrograph is shown to illustrate the manner in which the new single layer of epithelium grows on granulating bed beneath fibrinocellular membrane

HEALING PROCESS IN CLOSED ANASTOMOSES COMPARED WITH OPEN METHODS

The rate and manner of healing of gastrointestinal wounds made aseptically with the

actual cautery compare favorably with other methods The aseptic procedures used in these experiments apparently will result in mucosal healing in 14 to 17 days, while portions of the anastomosis may be epithelialized in eleven days There are ample opportunities to compare these results with the findings of others who have experimented with open anastomoses Gould, for example, found that the average time for mucosal healing in experimental gastrointestinal anastomoses was 14 days Flint came to the same conclusion after studying comparative rates of healing with the use of three different methods of suturing The more comprehensive study by Martzloff and Suckow (9) showed healing in 6 days in 2 anastomoses in which Halsted presection sutures were used When the same authors used the Connell suture they found epithelialization by a single layer in one 14 day specimen and incomplete coverage in another They also reported mucosal union in one of two 14 day specimens in which the commonly employed continuous hemostatic suture was utilized Healing with this method, however, was attended by intense inflammatory reaction, irregular mucosal defects, and frequent inclusion cysts

When healing at the line of apposition is used as a yardstick, the closed method compares to even better advantage The fact that all of the specimens showed the healing process to be a proliferative one attests to the advantage of preventing soiling by the use of an aseptic procedure

CONCLUSIONS

- 1 The healing in 17 aseptic anterior gastroenterostomies and 10 aseptic gastric resections, experimentally produced in dogs, was studied

- 2 Hemorrhage was most effectively prevented by leaving a seared 3 millimeter cuff of tissue protruding above the clamp after resection of the stomach or intestine had been carried out

- 3 The mucous membrane healed in 14 to 17 days

- 4 The usual microscopic picture of the healing at the line of apposition was a proliferative one

TABLE I.—RESULTS OF EXPERIMENTS

Case No.	Days of catheter drainage	Duration of clearance test (hrs.)	Inulin clearance	Phenol red clearance	Phenol inulin/phenol ratio
79246			80 160	150 161 144	
			13 17 80	30 170 141	
	10		100 100 83	100 114 100	
		3		11 30 114 110 107	
	10		17 17	174 160 170	
177			90 14 97 104	166 17 111 110	
			16 10	90 100 100	
			90 90 104	110 111 113	
	6	3.0	90 17	110 100 110	
			100	114 111	
1507			10 11 10	117 113 110	
	1.6		90 11 101	100 110 104	
		3.0	100 90 90	110 117 100	
	8		90	111 100	
	16		100	100	6

*Blood sample hemolyzed

TABLE II.—COMPARISON OF PHENOL RED AND INULIN CLEARANCES

Case number	Mean percentage recovery of inulin clearance following drainage	Mean percentage recovery of phenol red clearance following drainage
3	26	41.8
4	9	11.7
5	10.0	16.1
6	15	4.7
	8	17
		9
Average	14.6	11.8

that a blue compound results from the combination of diphenylamine and a polysaccharide in the presence of hot concentrated hydrochloric acid. Colorimetric readings were made a single cell compensating photoelectric colorimeter of Evelyn, and No. 650 filter being used.

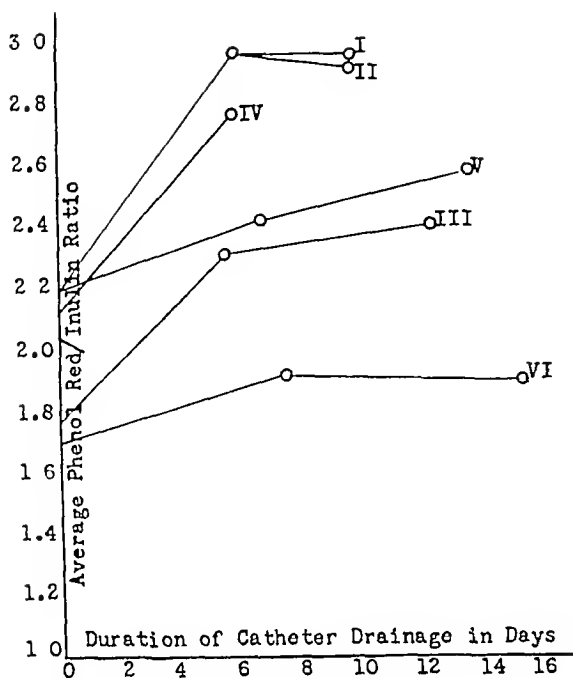
Phenol red determinations were made colorimetrically and the same type of photoelectric colorimeter with a No. 550 filter was used. A standard curve was first prepared the known concentrations of dye solutions being used and the unknown experimental concentration was read directly from the curve.

In the execution of phenol red clearance tests there are several essential points. The plasma concentration of the dye must be maintained at a level below 10 milligram per cent. When plasma dilutions are made the alkali must never be added to the plasma until after dilution otherwise precipitation will result with its concomitant false colorimetric values. The inherent chromogenic properties of the plasma must be compensated for in the colorimeter and each sample of plasma must be tested for hemolysis (Bling and Baker).

Interpretation of the experimental results
The tabulated results (Table I) demonstrate that continuous vesical drainage improves total renal function in prostatism. However no apparent relationship between the length of vesical drainage and the amount of renal functional improvement could be demonstrated. That is, improvement was dependent upon the amount of actual damage that occurred before the establishment of drainage and this no doubt must be dependent upon the duration of symptoms. Case 6 (Table I) with its limited functional improvement, though drainage was continuous over a 16 day period suggests this conclusion.

concentration in milligrams per cent. B=mean plasma inulin or phenol red concentration per cent. and V=urine volume in cubic centimeters per minute.

The method of measuring quantitatively the amount of inulin in plasma and urine was that described by Corcoran and Page. In principle this method makes use of the fact



Graph 1 Total renal function continues to a certain point and then ceases

The phenol red/inulin ratio was incorporated in the table since it more accurately represents renal function (Goldring, Clarke and Smith). The normal phenol red/inulin ratio is 3.3. That the ratio more nearly represents the true index of renal activity was demonstrated in Case 1 (the third hour of the clearance rate period on the tenth day of catheter drainage). Here it is seen that the clearance rate for inulin is 93 cubic centimeters per minute (normal 125 cc) and the phenol red clearance is 289 cubic centimeters per minute (normal 400 cc). These two figures would seem to indicate markedly impaired renal function though when the phenol red/inulin ratio is examined it is found to be 3.1 as compared to 3.3 which is normal. Hence, renal function is in this particular instance not impaired as seriously as one would be led to believe by examining the clearance rates separately.

Upon examination of Table II it is seen that phenol red clearances seem to have improved relatively more than the inulin clearance. From these figures the improvement of the tubule function, as compared with that of

the glomerulus, occurred in a ratio of approximately 2:1. Obviously to establish this as factual a larger series of cases will have to be investigated. It can be said then, in the final analysis of the experimental results obtained in this study, that renal function was improved following prolonged periods of vesical drainage in prostatism and that the increase was apparently more pronounced in the tubule than the glomerular elements of the kidney.

Graph 1 demonstrates that the improvement of total renal function continues to a certain point and then ceases, that is, apparently renal damage is reversible to a certain point and after that is irreversible. Just what determines the degree of irreversibility was not determined. However, this factor of reversibility of renal functional damage has long been appreciated by urologists and the stationary period (the plateaus on the graph) has been loosely termed "renal stability" and constitutes one of the principal criteria indicative of the optimum time for prostatectomy.

EVALUATION OF STUDY

The problem of renal dysfunction in prostatism has received little or no experimental investigation. In fact, careful search of the literature reveals no single reference dealing with this problem. Reference was made on occasion to the observed fact that renal function improved in prostatism with the institution of bladder drainage, but further than advocating this observation as significant as an operative index nothing could be found.

Strong studied the nephron by microdissection in experimental hydronephrosis and found that early in hydronephrosis the proximal convoluted tubule became markedly reduced in volume. Suzuki, using vital stains, found cells of the distal portion of the proximal convoluted tubules to be damaged before those in the initial portion of the tubule. Hinman, working with rabbits, found that the tubule suffered damage before the glomerulus. In these various experiments, the urinary back pressure, though created by different means was still in its early stages and from that point of view one might imagine at least, that the situation was somewhat comparable to the urinary obstruction of prostatism, and it is of

interest that the results of this work support these findings.

SUMMARY

1 Renal dysfunction was investigated by the use of simultaneous inulin and phenol red clearance tests.

2 Renal dysfunction in prostatism is primarily a tubule dysfunction.

3 The disturbed renal function in prostatism is definitely improved by continuous vesical drainage.

4 Renal damage due to prostatism is partially reversible. Re-establishment of renal function is not complete but reaches a peak

beyond which no further functional improvement occurs.

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THE EFFECT OF HEPARIN ON THE BEHAVIOR OF INFARCTION OF THE INTESTINE

An Experimental Study

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IN his recent reports (3, 4) Murray advocates the use of heparin following resection for infarction of the intestine. These reports have stimulated our attempt to determine the effect of this anticoagulant upon various types of mesenteric vascular occlusions and strangulations. The high postoperative mortality in cases of mesenteric vascular occlusion has been ascribed to the propagation or extension of small thrombi into larger vessels after operation. The question arises as to the value of heparin in enhancing the viability of the intestine whose circulation has been compromised by mesenteric vascular occlusion. Our experiments were conducted to study this problem and to determine under what conditions it is safe to administer heparin.

METHOD

The circulation of the small intestine of the dog was impaired in 4 ways: (1) ligation of mesenteric vessels, (2) the injection of 2 per cent sodium ricinoleate¹ into the mesenteric vessels to produce slow thrombosis, (3) the injection of fibrinogen² into the mesenteric vessels to produce rapid coagulation and (4) strangulation of loops of intestine. Heparin³ was administered in some instances before the lesions were produced and shortly afterward in others. In each instance a control series of experiments was conducted, in which no heparin was administered.

Heparinization was maintained for varying periods of time up to 7 days. The multiple injection method was used, except in a few instances.

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¹ Ricinogen, Tissue Phosphorylase and cephalin in sterile suspension.
² Heparin, 1% solution in 0.9% sodium chloride solution.
³ Heparin, 1% solution in 0.9% sodium chloride solution.

stances in which continuous venoclisis was administered overnight. The coagulation time was kept well above normal, but little effort was made to stabilize it at a constant level. It apparently made little difference in the results whether the coagulation time was slightly above normal or far above. A control coagulation time was taken before each experiment. Coagulation times after the administration of heparin varied from 10 to 45 minutes.

EXPERIMENTS CONCERNED WITH LARGE MESENTERIC VESSELS

In the first series of experiments the superior mesenteric vessels were ligated. The results of such ligations have been reported many times in the past. Scott and Wangenstein found that the average length of life following ligation of the superior mesenteric vein in dogs was 5½ hours, following ligation of the superior mesenteric artery, 20 hours, and following ligation of both artery and vein 19 hours. The results of control experiments were comparable to theirs.

The process of actual infarction is reversible up to 2 to 4 hours following ligation of the superior mesenteric vein and the animal usually survived if large quantities of blood were given by transfusion and the ligature released within this period of time. The blood volume ordinarily was reduced 50 to 60 per cent. Heparin, as might be expected, had no effect on the course of such animals. Because of the wide variation in survival times of control animals it was difficult to ascertain whether heparin actually hastened death by prolonging the coagulation time and allowing the animal to bleed more freely.

Ligation of the superior mesenteric artery in heparinized dogs produced the same end results as in the control series.

TABLE I—EXPERIMENTS CONCERNING SMALLER MESENTERIC VESSELS

Procedures	Experimental days	Result	Control days	Result
Devascularization of 10 to 20 cm small intestine by ligation		All survived, smooth abdomen		Death in 12 from gangrene and perforation in all and 70 hrs. One survived, active
Devascularization of intestine by ligation		Death in 12 hrs 6 days and days respectively		Femur dead after 12 and 48 hrs
1 cc 2% sodium picosulfate injected into mesenteric blood arteries, arches ligated on each side		One died after 48 hrs. survived		Death in 12 within 48 hrs.; (gangrene) Reaction of gangrenous segment done in 12 after 24 hrs. died from peritonitis
Chromogen injected into mesenteric blood arteries, arches ligated on each side		Death within 12, 4, 24 and hrs. respectively (gangrene)		Death within 8, 12, and 24 hrs. respectively (gangrene)

Rapid thrombosis of the superior mesenteric vein was produced by placing a rubber guarded clamp on the vein near the junction with the portal vein. Five cubic centimeters of fibrinogen was then injected into the superior mesenteric vein distal to clamp and the clamp removed in 10 minutes. The mesenteric vessels became obstructed by a thick coagulum. The course of such animals was similar to that of those in which ligation was done. Heparin had no influence on the lesion.

Slow thrombosis of the superior mesenteric vein was produced by injecting 0.5 cubic centimeters of 2 per cent sodium picosulfate solution distal to a rubber guarded clamp as described. When the clamp was removed after 20 minutes the cyanotic, relaxed appearance of the intestine due to clamping rapidly disappeared with the onset of hyperperistaltic contractions. A return of color gave one the impression that viability was assured. The abdominal wall was then closed. However a thrombus formed within the damaged vessel propagated postoperatively and caused death within 24 to 48 hours. Postmortem examination revealed massive hemorrhagic infarction of the intestine due to thrombosis of the superior mesenteric and portal veins.

In 3 of 5 such animals in which heparinization was maintained for 5 to 7 days, thrombosis was prevented, and they lived with no apparent ill-effects. The 2 other dogs died in 48 and 60 hours with hemorrhagic infarction of the intestine. In 2 other animals the administration of heparin was stopped after 24 hours, and these animals died several hours later from infarction due to mesenteric thrombosis. Apparently the heparin had not been

continued for a long enough period of time to prevent eventual thrombosis and death.

EXPERIMENTS CONCERNED WITH SMALLER MESENTERIC VESSELS

Welsh and Mall demonstrated that if more than 5 centimeters of intestine are deprived of blood supply gangrene results. Similarly Elsberg found that in the dog's intestine there is sufficient anastomosis of the intramural vessels in the longitudinal axis to supply at least 5 centimeters of uncontracted intestine if the vasa recta to such a segment are obstructed. In order to deprive a longer segment of its blood supply care must be taken to ligate all vessels from adjoining vascular arches, including those immediately adjacent to the serosa, as well as main vessel to that segment.

When the vessels supplying 10 to 12 centimeters of intestine were ligated, 2 of 3 control animals died from gangrene of the segment and peritonitis in 48 and 70 hours, respectively. The third showed no apparent ill-effects. The 3 animals treated with heparin for 5 days all lived and remained well. Subsequent laparotomy on the surviving untreated animal showed more extensive adhesions than in the animals treated with heparin. The anticoagulant thus permitted the survival of a segment of bowel 10 to 12 centimeters in length after occlusion of its extramural blood supply. The death of the control animals confirms the fact that in the dog a segment of bowel 10 or 12 centimeters in length usually cannot survive when devascularized. It is possible that the anticoagulant by preventing thromb from forming in the intramural vessels, allows for more extensive collateral cir-

TABLE II—STRANGULATION EXPERIMENTS

Control series			Heparin series		
Time strangulated hrs	Length of intestine ft.	Result	Time strangulated hrs	Length of intestine ft.	Result
3	1	Recovery	3	1	Death Hemorrhage 24 hrs (found dead)
3	1	Death Peritonitis due to evisceration 72 hrs	3	1	Recovery
6	1	Recovery	6	1	Death Hemorrhage 24 hrs (found dead)
6	1	Recovery	6	1	Death Hemorrhage perforation and peritonitis 24 hrs (found dead)
3	2	Recovery	3	2	Death Hemorrhage 24 hrs (found dead)
3	2	Recovery	3	2	Death Hemorrhage 24 hrs (found dead)
6	2	Recovery	6	2	Death Hemorrhage 24 hrs (found dead)
6	2	Recovery	6	2	Death Hemorrhage 12 hrs
6	2	Recovery	6	2	Death Hemorrhage 12 hrs

culation from the normal bowel on either end. If increased bleeding occurs following heparin, apparently the blood loss from a short segment before recovery sets in is not sufficient to cause death.

When the vessels supplying 15 to 20 centimeters of small intestine were ligated, heparinization did not permit the survival of the segment, although these animals lived somewhat longer than did the control animals. All died within 5 days with gangrene of the deprived segment and peritonitis. None of the control animals lived longer than 48 hours, while the survival periods of the 3 heparinized dogs were 72 hours, 4 days, and 5 days, respectively. Blood loss was no doubt increased, but did not account for death in these animals. This experiment would indicate that a segment of bowel of 15 to 20 centimeters is apparently too long to allow collateral blood supply to nourish the entire segment from either end when the extramural blood supply is cut off.

Slow thrombosis of medium sized mesenteric vessels was produced by the injection of 0.5 cubic centimeter of 2 per cent sodium ricinoleate into such an artery distal to a clamp which included both artery and vein. This resulted in spasm of the involved segment of bowel, already cyanotic from the clamping. Removal of the clamp after 20 minutes was immediately followed by an apparent return to normal color. Palpation revealed pulsations in the vasa recta, and

hyperperistalsis was marked. It seemed that the bowel would survive. However, each of 4 such dogs showed infarction of the segment within 24 hours, and, unless the segment was resected, died within 48 hours.

The same experiment was carried out on 5 dogs which were heparinized at the time of injection and kept heparinized for 5 days. Four of the 5 animals survived. When the surviving dogs were reopened 1 or 2 weeks later, the omentum and neighboring intestinal loops were found closely adherent to the involved segment and its mesentery.

Rapid thrombosis of medium sized mesenteric vessels was produced by injecting 2 cubic centimeters of fibrinogen distal to a clamp, as described. Although a coagulum formed within the vessels within a few minutes, the survival times of 3 such animals varied from 8 to 24 hours. The 4 heparinized animals in which this procedure was done lived from 12 to 48 hours. Heparinization may have thus prolonged life to a certain extent, but did not prevent infarction and death in animals in which rapid thrombosis was produced.

STRANGULATION EXPERIMENTS

Scott and Wangenstein found that the length of bowel involved in strangulation is a factor in determining the survival period. Aird and others have emphasized other factors which play important rôles in the cause of death following low intestinal strangulation obstructions. It has been shown that in

short loop strangulations death is usually due to perforation and peritonitis. In strangulations of medium length death is apparently due to the absorption of certain toxins. In long-loop strangulations death is due to diminution in blood volume resulting from blood loss into the lumen and wall of the strangulated intestine and into the peritoneal cavity.

Our strangulation experiments were concerned with determining the effect on the recovery of medium lengths of gut strangulated for varying periods of time up to 6 hours. It was felt that release of the strangulation within this period would not allow the lethal factors associated with low intestinal strangulation obstruction to be effective.

Four groups of strangulations were carried out by means of binding tape (Table II). In each group a control series of dogs was compared with a heparinized series. Fasting dogs of about the same weight were used, and an attempt was made to produce the same amount of vascular obstruction in each instance. The tape was first tied around the mesenteric stump and then around the loop of ileum to be obstructed and was pulled as tight as the tape would allow.

In most instances, when the tape was released after at least 3 hours, the bowel appeared questionably viable. In others, the infarction appeared irreversible. The bowel resembled that of the human during operations for strangulated hernia after incarceration for 12 hours or more. The segment was dark blue or black until released. It then became very red with purple or bluish areas in the wall and the lumen contained blood. The peritoneum contained a bloody transudate.

All but one of the control animals recovered after release of the strangulation and closure of the abdomen. The 1 death occurred after 72 hours and was due to peritonitis brought about by evisceration before strangulation was released. All but 1 of the heparinized dogs were found dead 24 hours after release of strangulations and closure of abdomen.

The cause of death in these animals was undoubtedly shock due to blood and fluid loss as evidenced by the large amount of bloody fluid in the peritoneal cavity and in the lumen

of the bowel. However, in one of the 6-hour 1-foot strangulations, death was due to perforation and peritonitis. The prolonged coagulation time following heparin apparently allowed free bleeding, thus increasing the amount of blood lost during the strangulation.

An observation was made during the strangulation experiments concerning the use of hot laparotomy pads in cases of questionable viability of the intestine. We wished to determine the safety of administering heparin after operation in such cases when resection was not done. Each of 4 dogs in which the bleeding points on a strangulated loop were controlled by means of hot laparotomy pads died from hemorrhage after heparin was administered. It was observed that the previously coagulated bleeding points began to bleed within 1 hour after injection of heparin.

RESECTION

We have performed several resections in the presence of heparinization. There was much more bleeding than is normally encountered, and much time was consumed for hemostasis. However, the procedure was satisfactorily completed in each case and the mortality following resection was no different than in control animals.

CONCLUSIONS

From our experiments it would seem that it is unsafe to administer heparin after operation in cases of impaired circulation of the intestine when resection is not performed. Although it appears that heparin enhances the chance of recovery of short devascularized segments, in cases of mesenteric vascular occlusion or strangulation it should be reserved only for those cases in which resection is performed.

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EXTRATHYROIDAL METABOLISM OF IODINE

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IODINE has been identified with the physiology of the thyroid gland since the findings of Chatin, Baumann, Marine, and others. These studies have tended to focus attention on the intimate rôle played by thyroid tissue in iodine metabolism. Reports of subsequent work on the function of iodine in the organism, for the most part, have assumed or implied the participation of thyroid tissue.

The recent experimental *in vitro* production of thyroxine or thyroxine-like substances by the iodization of protein has been accomplished. In view of the formation of these calorigenic substances in the absence of thyroid tissue, the effect of iodine on the completely thyroidectomized animal should be significant. The results of such observations form the basis of this report.

METHODS OF STUDY

For this investigation 42 male, albino rats aged 7 weeks and weighing approximately 165 grams were selected and divided into 2 groups. Twenty-four rats on which thyroidectomy was not performed formed 1 group and 18 thyroidectomized rats formed a second group. Thyroidectomy was complete in all animals but one in which a small amount of thyroid tissue was observed at necropsy.

All animals received the same goitrogenic, low iodine diet described by Remington, and all animals had free access to distilled water.

The groups of intact and thyroidectomized animals were each divided in half, 12 intact and 9 thyroidectomized animals each formed a group which received an iodine supplement. This was administered in the drinking water,

15 micrograms of iodine as potassium iodide per cubic centimeter of water, which supplied to these 2 groups, respectively, an average iodine intake of 34 and 27 micrograms per rat per day. Less than 5 per cent difference in the intake in the 2 groups existed, calculated on a basis of average body weight. Thus 4 groups of animals were arranged: 2 groups of intact animals, 1 receiving a supplement of iodine and the other on a low iodine intake, and similarly, 2 groups of thyroidectomized animals on supplemented and restricted iodine intake.

Body weights were recorded every third day and the consumption of food and water was measured and recorded daily. Respiratory metabolism was determined twice during the course of the experiment.

EXPERIMENTAL DATA

The data have been calculated and expressed in terms of unit weight and surface area of rat tissue because of the diverging weights of the different groups. Thus the food intake of a group of rats averaging 200 grams was compared properly with the food intake of a group averaging 150 grams.

Food and water intake and changes in body weight were observed from the fourth to the sixty-ninth postoperative day, thus constituting a 65 day experimental period.

The changes in surface area of these animals (Fig. 1) were based on the percentage change in weights from the onset of the experiment. Difference in the level of iodine intake made little change in the rate of growth of intact animals, but in thyroidectomized animals differences were observed. Those on restricted iodine intake lost weight and surface area more rapidly than the animals receiving the iodine supplement. The terminal rise of the growth curve (Fig. 1) in the thyroidectomized animals on low iodine intake is explained by the death of low weight members of this group, whereas the animals whose percentage loss of surface area was less survived.

A portion of thesis submitted to the Faculty of the Graduate School of the University of Minnesota in partial fulfillment of the requirements for the degree of Doctor of Philosophy. This study combined with the essay "The Relation of the Thyroid and the Pituitary Glands to Iodine Metabolism," was awarded the Van Meter Prize by the Association for the Study of Goiter.

Work done at the Institute of Experimental Medicine under the direction of Dr. G. M. Higgins.

Presented in the Forum on Fundamental Surgical Problems, Clinical Congress of the American College of Surgeons, Boston, November 3-7, 1941.

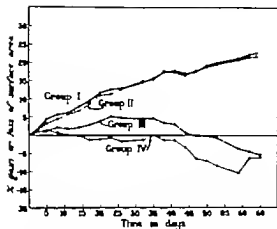


Fig. 1. Growth curves expressed as percentage changes in surface area. — Group I, intact animal, adequate iodine intake; — Group II, intact animal, low iodine intake; — Group III, thyroidectomized animal, adequate iodine intake; — Group IV, thyroidectomized animal, low iodine intake.

The actual changes in weight and surface area of the 4 groups (Table I) included the changes occurring during the life of the rats which died during the course of the experiment. These figures represent the net performance of the groups more accurately than the graph of percentage changes but they do not show the progressive changes so well. Again there was noted very little difference in the changes in weight or surface area in the 2 groups of intact animals receiving low and

TABLE I.—CHANGES IN WEIGHT AND SURFACE AREA THAT OCCURRED DURING THE EXPERIMENTAL PERIOD

Animals	Groups	Actual gain or loss over total period*		Average gain or loss per rat per day	
		Wt. gm.	Surface, sq. cm.	Wt. gm.	Surface, sq. cm.
Intact	I Adequate iodine	+9.50	+796	+.31	+.26
	II Low iodine	+8.66	+770	+.28	+.25
Thyroid-ectomized	III Adequate iodine	-.7	-.8	-.023	-.026
	IV Low iodine	2.2	51	-.052	-.077

*Changes in animals that died during course of experiment are included.

TABLE II.—INTAKE OF FOOD RELATION TO CHANGES IN SURFACE AREA

Animals	Groups	Food intake for group, gm.		Gain or loss of surface area per gm. food intake per sq. cm.
		Total	Average per sq. cm. of surface area per sq. lbs.	
Intact	I Adequate iodine	76	0.511	+.046
	II Low iodine	3.3	.01	+.048
Thyroid-ectomized	III Adequate iodine	2.76	.038	-.004
	IV Low iodine	1.8	.177	-.002

adequate iodine intake. But of the thyroidectomized animals, those receiving the low iodine diet without iodine supplement suffered a threefold loss of weight and surface area in comparison with those animals in the thyroidectomized group receiving an iodine supplement.

The food intake and the gain or loss of surface area in proportion to the food consumed were computed (Table II). The latter comparison represents a measure of food utilization. The food intake and its utilization by the 2 groups of intact animals were approximately the same. However among the thyroidectomized animals, although those receiving a low

TABLE III.—INTAKE OF WATER RELATION TO CHANGES IN SURFACE AREA

Animals	Groups	Intake of water			Gain or loss of surface area per cc. of water
		For group,		Ratio of, to intake of food ^a	
		Total	Average per sq. cm. of surface area per sq. lbs.		
Intact	I Adequate iodine	.960	.0704	+.022	
	II Low iodine	.461	.0640	+.046	
Thyroid-ectomized	III Adequate iodine	10.030	.0692	-.001	
	IV Low iodine		.0761	-.001	

*Ratio of cubic centimeters of water to grams of food.

TABLE IV—CALORIC INTAKE AS FOOD, BASAL CALORIC OUTPUT (CALCULATED FROM OXYGEN CONSUMPTION) AND PERCENTAGE DEVIATION OF METABOLIC RATES FROM THOSE OF CONTROL GROUPS

Animals	Groups	Average caloric intake or output per sq m per 24 hrs		Basal metabolic rate, percentage deviation from normal caloric output	
		Intake	Output (basal metabolism)	Basis 1032	Basis 588
Intact	I Adequate iodine	1922.4	1032	0	
	II Low iodine	1947.6	1090	+6	
Thyroid ectomized	III Adequate iodine	1378.8	588	-43	0
	IV Low iodine	1177.0	482 (432)*	-53 (-58)*	-18 (-27)*

*One animal with regenerated thyroid tissue (rate -30) was excluded

iodine intake consumed almost as much food as the controls receiving iodine, yet they lost more than three times as much weight and surface area. That is, the thyroidectomized animals that received iodine utilized their food better than the thyroidectomized animals which did not receive an iodine supplement.

A study of water intake in relation to surface area, to change in surface area and to the intake of food showed (Table III) that the water consumption in intact animals on either low or adequate iodine intake was not altered significantly. The water intake in thyroidectomized animals on low iodine intake, however, was significantly greater than in the thyroidectomized animals receiving iodine. This was evident in relation to surface area as well as to the food intake. For every gram of food taken by the thyroidectomized animals receiving supplemental iodine, 1.7 cubic centimeters of water was consumed, while the thyroidectomized group on low iodine consumed 2.4 cubic centimeters of water for each gram of food. The expression of loss of surface area in relation to water consumed indicates that the loss was approximately proportional to the loss calculated on a basis of food intake, that is even though the water consumption was greater, the loss in weight and surface area

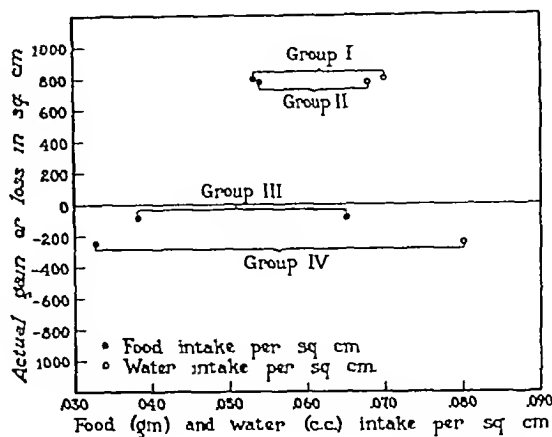


Fig 2 Relation of intake of food and water to change in surface area. The length of the brackets indicates the ratios of food to water intake in the groups

progressed. It is probable that the changes in weight and surface area were independent of the water intake and that the animal had diuresis and not retention of water. The relative differences in the amounts of food and water consumed and in the change in surface area of the 4 groups of animals are shown in Figure 2.

The metabolic rate of the animals was determined on the 49th and 64th days of the experimental period, a slight decrease in the oxygen consumption occurred in the second determination. The average of the two determinations was selected as a basis for comparison of the metabolic rates in the 4 groups (Table IV). A slight increase, 6 per cent, in the average basal metabolism of the intact (goitrous) animals receiving low amounts of iodine over that of the intact animals receiving adequate amounts of iodine may not be of sufficient magnitude to be significant. However, a real difference between the mean metabolic rate of the two thyroidectomized groups, with and without the iodine supplement, was observed. If the one animal in the thyroidectomized group which did not receive any iodine supplement and which showed regenerated thyroid tissue at necropsy was excluded then the basal metabolic rate for this group was depressed 27 per cent below that of the thyroidectomized control group receiving the iodine supplement.

Caloric value of the food intake of the groups was calculated (Table IV). However as this was not consumed under basal conditions the comparison with the caloric output is only relative.

EVALUATION OF STUDY

The presence of thyroid tissue in the intact animals permitted utilization of the small amount of iodine available in the low iodine diet. To accomplish this the thyroid hypertrophied, thereby maintaining the growth and well being of the organism, as shown in the growth curve of the two intact animal groups.

The thyroidectomized animals, on the other hand deprived of tissue especially adapted to the processing and utilizing of iodine, suffered a change in body growth and function. Unlike the intact animal groups, however the presence or absence of a plentiful supply of iodine made a distinct difference in the performance of the thyroidless animals. This was evident in the depressed growth curve the less efficient utilization of food, the greater intake of water and the distinctly lowered metabolic rate associated with the restricted iodine intake in the athyroid animal as compared with a similar group of animals receiving an iodine supplement. It is evident that iodine played some rôle in the body economy of the thyroidectomized animals.

The possibility that iodine may have an effect on vital processes in the absence of thyroid tissue was emphasized by the work of Swingle, Hoskins and Hoskins, Allen, and others who showed that iodine stimulated metamorphosis in thyroidectomized amphibians. Further evidence that iodine may affect growth processes in the absence of thyroid tissue was shown by Silberberg and Silberberg who reported stimulation of growth of bone in immature thyroidectomized guinea pigs by the administration of iodine. This resulted in a parallel to the growth of bone caused by the administration of thyroxine to thyroidectomized animals.

Abelin, Ludwig and von Mutszenbecher, Salter and Lerman, Block, and others have demonstrated the production of thyroxine

diiodotyrosine and calorigenic protein similar to thyroglobulin by the iodization of organic material *in vitro*.

It is possible that iodine in the thyroidless animal acted in a similar manner to that of iodine on organic matter *in vitro* possibly aided by enzyme action not necessarily confined to thyroid tissue. This effect of iodine in the thyroidless animal, then, may represent the action on the tissues of a certain concentration of iodine, thus elaborating a thyroxine-like substance.

If an extrathyroidal utilization of iodine exists, then its function in disease associated with iodine metabolism may be significant, especially in hypothyroid states. The untoward effects of iodine lack in the athyroid animal suggest that an absolute iodine deficiency would impose a more severe strain on the organism and that life itself may not be compatible with the complete absence of iodine.

SUMMARY AND CONCLUSIONS

A difference in iodine level in the diets of thyroidectomized rats significantly altered the changes in weight and surface area, the water intake, the food utilization, and the metabolic rate. These changes were not induced in the intact animals by deprivation or administration of iodine.

From the data presented it is concluded that iodine may play a rôle in body metabolism in the absence of thyroid tissue, possibly by the production of a thyroxine-like substance in the tissues.

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THE DIAGNOSIS AND TREATMENT OF CANCER OF THE STOMACH

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BECAUSE cancer of the stomach has received so much attention in recent years, further comment at this time would seem to be superfluous. Several extremely discouraging facts stand out so vividly, however, that one is justified in reviewing the present status of the problem as it is obvious that even greater efforts will have to be expended if any appreciable improvement is to be achieved in the early diagnosis and treatment of cancer of the stomach.

The seriousness of cancer of the stomach may be emphasized by comparison of the 5 year survival rates of all patients who have a malignant lesion in the more common sites, whether treatment has been given or not. With the possible exception of primary carcinoma of the lung, the 5 year survival rate after the diagnosis of cancer of the stomach is appreciably lower than the 5 year survival rate in cases in which a diagnosis of cancer of the fundus of the uterus (55 per cent), thyroid gland (42 per cent), breast (32 per cent), uterine cervix (31 per cent), or large intestine (24 per cent) has been made.

Walters, Priestley, and I have reported elsewhere the results of the study of a large group of cases of malignant lesions of the stomach. From a study of these cases, it was noted that of all cases in which a diagnosis of a malignant lesion of the stomach had been made, operation was performed in only 57.7 per cent (surgical rate) and that resection of some type was possible in only 25.8 per cent. The immediate hospital mortality in the group of cases in which resection was performed was 16 per cent, which, when translated into terms referring to the total number of patients observed, reduces the number of patients who theoretically have any chance of survival to 21 persons for each 100. In 28.9 per cent of cases in which a malignant lesion of the

stomach was successfully treated by resection the patients were found to be alive at the end of 5 years, whereas only 6.2 per cent of the total number of patients observed with a malignant lesion of the stomach were alive at the end of the same period.

It is interesting to note the similarity in the operability rate and resectability rate in 127 cases of primary carcinoma of the lung reported by Overholt. In 41 per cent of the cases the lesions apparently were operable but in only 26 per cent of the cases exploratory operation disclosed the lesions were operable. At the time Overholt made the report, in 11 per cent of the cases in which the patients were living in which the malignant lesion had been removed, there was no evidence of metastatic involvement. It is impossible to determine at this date the 5 year survival rate as only 3 of 13 patients with no evidence of metastasis had been operated on more than 5 years before the report was made, and for this reason it is obvious that the 5 year "salvage" rate for the total number of patients observed will be appreciably less than 11 per cent and probably will be very close to that already mentioned for malignant lesions of the stomach.

The fact that early removal of a malignant lesion of the stomach is the only known method of cure has been emphasized repeatedly and is so widely accepted that repetition at this time seems trite and elementary. It may be assumed that because our study has been based on all cases of malignant lesions of the stomach observed in the years 1907 to 1938, inclusive, the surgical rate of 57.3 per cent and the resectability rate of 25.5 per cent will be low when compared to similar figures based on experience during the last 15 years. Unfortunately, such is not the case. The ratio of patients operated on to total patients who were found to have a malignant lesion of the stomach has varied

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little during the last 15 years from the surgical rate for the whole period and although the ratio of patients who underwent resection to the total number of patients is slightly higher than the rate of 25.5 per cent, the improvement is so insignificant as to be negligible.

The answer to this difficult and discouraging problem is not easy. One of the first responsibilities of the medical profession is to spread the knowledge that, with proper care, cancer of the stomach (in the broad sense) can be cured if it is attacked when the process is in its early stages and is localized in the stomach. That the symptoms of cancer of the stomach may be vague and ill defined is well known. Laymen must understand that there is no typical symptom complex that is characteristic of cancer of the stomach, and the physician and surgeon likewise must not wait for the development of characteristic symptoms before considering the possibility of the presence of a malignant lesion of the stomach and insisting upon a thorough examination in order to arrive at a correct diagnosis.

An attempt was made to classify the symptomatological picture presented by the patients who had cancer of the stomach in the group previously mentioned. This proved to be a difficult task because of the great variety of detailed symptomatological aspects inherent in such a large series of cases. The "unusual" type of symptomatological picture of a malignant lesion of the stomach occurred in three fifths of the cases and consisted of a symptom complex in which dyspepsia was the most prominent symptom and was associated with varying degrees of decline. Thirty per cent of the patients portrayed the symptomatological picture of "ulcer" which was characterized by epigastric pain occurring characteristically when the stomach was empty and which was relieved by the ingestion of food or alkali. Seven hundred ninety three patients who had a malignant lesion of the stomach had received some type of therapy for ulcers and 81 per cent of these patients had experienced definite subjective improvement. The observation would seem to discredit the value or the advisability of the use of the response to treatment as a criterion for distinguishing a malignant lesion from a be-

nign ulcer except under the most nearly accurate conditions of observation, which it is possible to obtain.

A reason for the discouragingly low surgical rate in cases of malignant lesion of the stomach has been suggested by the supposed frequency with which such lesions manifest themselves at such an advanced stage of development that the lesion is inoperable before the patient experiences symptoms which suggest its presence. That this occurs occasionally is well known. That this occurs frequently is not substantiated by the fact that only 18 per cent of this large group of patients had noted the first symptom referable to the stomach less than 3 months prior to their admission to the clinic whereas exactly half of the patients stated that they had experienced symptoms referable to the stomach for more than a year. It should be noted especially that the fact that a patient may have had symptoms referable to the stomach for a long time is no criterion upon which to exclude the presence of a malignant lesion of the stomach.

Among laymen, and particularly among physicians, there has been a lamentable lack of appreciation of the malignant potentiality of gastric ulcer. This statement does not suggest that all malignant lesions of the stomach start as benign ulcers. It is impossible from a pathological or clinical standpoint to determine how frequently this may occur perhaps not over 10 per cent, perhaps never. It is not really so important to quibble as to whether or not a particular malignant lesion was once a benign ulcer as to attempt to determine immediately whether or not the lesion under consideration is malignant. Through bitter experience it has been learned that there is no method by which an unequivocal clinical diagnosis may be made as to the malignancy or benignancy of any ulcerating lesion of the stomach. In spite of the fact that the most outstanding advances in the diagnosis of cancer of the stomach can be attributed to roentgenology and gastroscopy and that all other diagnostic methods in comparison become so insignificant that their importance can be disregarded, expert roentgenologists and gastroscopists admit that it is impossible in many instances to distinguish between a small ul-

cerating carcinoma, a malignant gastric ulcer, and a benign gastric ulcer. In our experience at the Mayo Clinic, approximately 9 per cent of carcinomatous ulcers had been diagnosed as benign by a roentgenologist, and what is even more significant, in 18 per cent of all cases of cancer of the stomach in which roentgenologic diagnosis was made, it was not possible to determine the exact nature of the lesion, and in 7 per cent of the cases a diagnosis of benign ulcer was made. It is particularly significant that some type of abnormal lesion of the stomach was noted in 99 per cent of cases in which a malignant lesion of the stomach was present. The fact that it is impossible to determine definitely by means of roentgenologic or gastroscopic examination the exact nature of certain lesions of the stomach is not surprising. This statement is not a criticism of either of these diagnostic methods. The two methods of examination of the stomach are supplementary and in many instances either one or the other may demonstrate an abnormal condition in the stomach while the remaining method may produce essentially negative results. A similar experience was recorded by Allen and Welch in a paper read before the American Surgical Association this year. This study dealt with 277 cases in which a surgical diagnosis of gastric ulcer was made. In 35, or 14 per cent, of the cases the lesion finally proved to be cancer. From this study, Allen and Welch have seen fit to recommend operation if (1) the gastric ulcer is of short duration and the patient is more than 50 years old, (2) the ulcer is more than 2.5 centimeters in diameter, (3) there is no free hydrochloric acid in the gastric contents, (4) the ulcer is situated on the greater curvature or in the prepyloric region, (5) the ulcer is chronic and is on the lesser curvature. They recommend hospital observation and treatment for 1 month if (1) the ulcer is acute and the patient is young, (2) the ulcer is less than 1 centimeter in diameter, (3) the ulcer is on the lesser curvature or on the anterior or posterior wall. If healing of the ulcer is complete in 1 month they said that repeated observation should be made 1 month after dismissal of the patient from the hospital. If healing is not complete in 1 month, as deter-

mined by roentgenologic and gastroscopic examination, then operation is advisable. My associates and I are in complete agreement with the principles of these conclusions. The fact cannot be emphasized too strongly however, that although the ulcer may give every evidence of having healed roentgenologically, gastroscopically, subjectively, and by the disappearance of occult blood from the stools, a malignant lesion may be demonstrated within a very few weeks after the fulfillment of these accepted criteria for a benign lesion.

TREATMENT

The purpose in treating cancer of the stomach is two-fold. The first is to effect a cure, if possible, and the second is to prolong life and reduce to a minimum the suffering which may be associated with the disease. It is obvious that the first purpose can be accomplished only by extirpation of the malignant mass together with accessible lymph nodes that are involved, including all of those in the greater omentum. In most instances, as shown by Carman, the question of operability, from the roentgenologic standpoint, depends on the situation, the extent, and the character of the cancer. He divided the stomach into 3 zones: the operable zone, corresponding to the pars pylorica, the borderline zone, corresponding to the pars media, and the inoperable zone, corresponding to the pars cardiaca. Tumors that are inoperable are usually situated in the cardiac end of the stomach, or have spread from a pyloric or fundic position to within the inoperable zone. Only rarely is a preoperative report of inoperability of a lesion in this situation not confirmed when exploratory operation is performed.

Roentgenologic evidence alone, however, should not be sufficient evidence in occasional cases to deny the patient what benefit may be derived from surgical exploration. This is particularly true of lesions situated primarily in the fundic portion of the stomach or near the cardiac orifice, as great strides have been made in the transpleural approach to these lesions. Although improvement in the "salvage" rate of patients with malignant lesions of the stomach may be expected with

the development and refinement of the more extensive surgical procedures a more promising field undoubtedly exists in widespread promulgation of the importance of early diagnosis and recognition of the malignant po-

tentiality of every ulcerating lesion of the stomach

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USE OF FEMALE SEX HORMONES IN CLINICAL PRACTICE

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ENDOCRINOLOGY during the past decade has been a veritable handmaiden of gynecology. Despite a widespread and often uncritical or ganotherapeutics, which has not failed to draw repeated criticism from conservative clinicians, securely established indications have now been delineated for the use of the newer hormones in everyday practice. Equally if not more important, contributions of endocrinology however have been manifest in the resultant evolution of a newer and more physiological approach to the handling of many of the ills of woman which emphasizes diagnosis of functional levels and has as its desideratum the utmost salvage of function and the preservation or restoration of the fertile state when it is possible. There is now less recourse to function-destroying surgery and roentgenotherapy unless it is founded upon securely established indications.

The ovary elaborates two kinds of female sex hormones *estrogenic substances* (*estrogens*) from the granulosa cells of maturing graafian follicles and also from the cells of the corpus luteum and *progestational substances* (*progestin*) from the luteal cells of the corpus luteum. *Estrogens* are responsible for the manifold definitive changes in the sexual apparatus, and elsewhere which characterize the adolescent epoch of sexual maturation and for the maintenance during the reproductive years of a state of development in the sexual organs compatible with the functional re-

quirements placed upon them. These hormones are largely responsible therefore for the objective and subjective femininity of woman. *Progestin* is concerned with the preparation of the uterus in particular and the woman in general for the monthly physiological anticipation of pregnancy and when gestation does occur with important roles in the nutrition and protective sheltering of the developing fetus. Opposing to some extent and perhaps, also acting as synergists or pacemakers to these female sex hormones, are the contrasexual *androgenic* hormones which are elaborated in woman solely by the adrenal cortex. Woman's hormonal moiety must be viewed then as being dual in sexual nature as Blair Bell has observed the older view that *propter ovarium solum mulier est quod est* is less a real statement of fact than *propter secretionem internas totas mulier est quod est*.

All of the ovarian and cortical adrenal hormones are steroids, or higher alcohols, which contain in common the cholane nucleus. Three different estrogenic hormones have been identified in woman's urine estrone, estrinol, and estradiol. Commercial preparations of all of these are available for therapeutic usage. These estrogenic hormones should be contrasted with certain nonhormonal drugs which possess estrogenic properties, but which have no chemical relationship to the natural steroids, for example diethylstilbestrol and its esters. During recent months diethylstilbestrol has been released into commerce by the Food and Drug Administration. Only one active progestational hormone, *progestin*, has been recovered in small amounts from woman's ovaries and urine. Another progesta-

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tional steroid, anhydro-oxypregesterone, has been prepared synthetically from estradiol. Both of these progestational steroids are available commercially. While four 17-ketosteroids of adrenal origin have been recovered from a woman's urine, androsterone, dehydroisandrosterone, isoandrosterone, and etiocho- lanol3(a)-17-one, only two of these, androsterone and dehydroisandrosterone, possess significant masculinizing or androgenic properties (2). Only the androgens, testosterone, which has been recovered from testes but not from urine, and its derivative, methyl testosterone, are used therapeutically.

USES OF ESTROGENS

Consideration of the known pharmacological properties of estrogens has justified as rational their trial under the following circumstances (9) (1) in certain established instances of estrogenic ovarian failure, occurring in adolescence or during sexual maturity, as substitutional or complementary therapy, (2) in certain subjective disturbances of the character as palliative but not full substitutional therapy, (3) in hypomastia for cosmetic effects alone, (4) in certain hyperfunctional states of other glands, i.e., the pituitary or adrenals, as antagonistic therapy, and (5) in certain cases for specific pharmacological effects upon the vaginal epithelium, the indication for therapy not being any endocrine disturbances.

In addition to these apparently rational indications, estrogens have been employed empirically and often contraphysiologically under various conditions.

Substitutional therapy in intrinsic ovarian failure. When severe grades of estrogenic failure of this character exist, the indication for therapy concerns the completion of sexual maturation in the adolescent and the prevention or correction of sexual regressions in the adult. Large doses of estrogens will produce dramatic endocrine responses under these circumstances, for the endocrine function of the ovaries can be substituted for just as effectively as that of the pancreas or the thyroid. Three important facts limit the practicality of prolonged substitution at the ovarian level (1) the expense involved the large dosages of

estrogens required day after day and year after year have imposed in the past an almost insurmountable financial burden, but the commercial availability of diethylstilbestrol has now circumvented this limitation, (2) the inability to overcome the sterility of the patient the germinal function of ovaries cannot be substituted for, and (3) the temporary nature of the results obtained regressions which erase, for the most part, all therapeutic results, occur when treatments are discontinued.

Fortunately, in view of these limitations, severe estrogenic deficiency rarely impairs health or somatic efficiency despite the cosmetic inelegancies it may impose upon the adolescent or the young woman. A limited trial of substitutional therapy is justified in the young woman with severe estrogenic deficiency upon the following grounds (1) to attempt to curb the abnormal somatic overgrowth of these young patients by effecting epiphyseal closures, a therapeutic hope not definitely established as a fact, (2) to bring about some degree of sexual attractiveness of the patient, for its salutary psychic effects, and (3) to alter beneficially the ovario-uterine reciprocities of these patients by the resulting genital growth and development (9).

Complementary therapy in intrinsic ovarian failure. Intercurrent episodes of intrinsic ovarian failure occur, as for example, the occasional sterile (anovulatory) cycles which even normal, healthy women may have. A preponderance of these may produce sterility and eventual distressful menstrual irregularities. Frequently excessive or prolonged uterine bleeding of the young woman is due to these intercurrent episodes of lowered receptivity of the ovaries to gonadotropic influences from the pituitary. The employment of a system of cyclic steroid therapy embracing the use of estrogens and progesterone under these circumstances permits effective control of the uterine bleeding without any further damage to ovarian function, in fact, not infrequently, this therapy may permit tiding the patient over this ovarian crisis until such time when normal function returns (11). Without such supportive therapy, doubtless many of these

intercurrent episodes progress to graver degrees of ovarian failure.

These statements regarding the effectiveness of the hemorrhagenic hemostatic schedule permitted by cyclic steroid therapy should not be construed as representing the advocacy of endocrine therapy solely to regulate the menstrual cycle. Many menstrual irregularities are innocuous, if not actually fanciful and endocrine therapy under these circumstances is meddling and often contraphysiological.

Palliative therapy in the physiological estrogenic failure of the climacteric. It is trite to state that estrogenic deficiency is physiological at the time of the climacteric, yet some of the massive doses of estrogens given at this time of life by some organotherapeutic enthusiasts would indicate apparent ignorance of the normal hormonology of this epoch. No need seems to exist for prolonged therapy with full substitutional or even larger dosages of estrogens at the time of the climacteric. Our knowledge of geriatrics has not reached such a state that we are justified in trying to postpone sexual aging.

All estrogenic therapy during the climacteric should fulfill this general therapeutic desideratum to lessen, but not to substitute for the physiological ovarian deficit of those women in whom severe subjective symptoms characterize this epoch, i.e. palliative not full replacement therapy. Therapy should be limited if possible in duration to several months dosages should be kept small and estrogens should be given orally if possible. If patients to be treated continue to have episodes of bleeding therapy should be adjusted cyclically so that it is withdrawn at the time of and during episodes of bleeding lest troublesome menstrual irregularities be added to the other symptoms of the patients.

Cosmetic therapy of hypomastia. A general statement regarding isolated hypoplasias of the genital system seems advisable at this time. When a woman who is apparently endocrinally adequate otherwise has unilateral or bilateral hypomastia or a hypoplastic uterus, the likely diagnosis is a faulty end-organ or end-organs rather than faulty ovarian function. Estrogenic therapy under these circumstances is usually of no benefit.

At times a patient with typical adolescent hypo-ovarianism is concerned solely by her hypomastia. The use of estrogenic ointments by local massage applied to the breasts may give gratifying temporary results if rather large doses of estrogens are employed and some permanent benefits may result, probably due chiefly to massage. It has been reported that the concomitant use of progesterone by injection lessens the regressions which follow the discontinuation of estrogens.

Antagonistic therapy of hyperfunctional states of other glands. Theoretical considerations have suggested that large doses of estrogen given over prolonged periods may offer a means of depressing hyperfunctional states of the pituitary and of nullifying the virilizing effects of hyperactivity of the androgenic elements of the adrenal cortex. The results of estrogenic therapy in neither of these conditions have been satisfactory despite the fact that it seems well established that the moderate gonadotropic hyperactivity of the pituitary which characterizes the climacteric is reduced by adequate estrogenic therapy. Larger dosage and more prolonged usage of estrogens permitted by recently available diethylstilbestrol may have better results.

Therapy for local vaginal effects. The special trophic effects of estrogens upon the vaginal epithelium have permitted effective applications in the treatment of gonorrheal vaginitis of childhood and of nonspecific postmenopausal vaginitis. Since hypoestrogenism is physiological at these two periods of life estrogens do not fulfill the requirements of hormonal agents but rather of active substances having a desired local action: the production of vaginal cornification and increased vaginal acidity both of which effects augment the resistance of the host to the invading organisms. Since estrogens are active when applied directly to the vagina, and since large doses are not required undesired general effects of this therapy (precocious adolescent phenomena and uterine enlargement with return of uterine bleeding, respectively for the two classes of patients) may be avoided.

Good results have been reported by some gynecologists from the local use of estrogens before operation in postmenopausal women.

awaiting plastic vaginal procedures. The modus operandi of this therapy is similar to that in vaginitis. The improvement in vaginal proliferation has been said to facilitate operation and postoperative healing.

Empirical and contraphysiological therapy
Time does not permit even a listing of the various empirical and contraphysiological uses to which estrogens have been put. Most of these have been concerned with the treatment of subjective symptoms, by fact or theory, usually the latter, related to disordered ovarian function.

An explanation is due, perhaps, in regard to our meaning of contraphysiological therapy. When estrogens are used in large doses in women with apparently normal ovarian function with the hope that ovulation and corpus luteum function can be prevented, which has been stated to be the rationale of such therapy in dysmenorrhea and "menstrual migraine," this in our opinion constitutes contraphysiological therapy.

Recently another type of contraphysiological therapy has been reported. Dunn has given male criminals with abnormal sexual histories large doses of diethylstilbestrol for the purpose of depressing the endocrine function of their testes. He was apparently quite successful and, in addition, observed markedly degenerative changes in their seminal tubules.

USES OF PROGESTERONE

All of the therapeutic applications of progestin (progesterone) and anhydro-oxypregesterone have been concerned with the substitution for or the complementation of corpus luteum failure during the progestational phase of the menstrual cycle or during pregnancy. In the first category, the following conditions come up for discussion: dysmenorrhea, estrogenic bleeding, and ovarian sterility, in the second instance, repeated or threatened abortions.

Dysmenorrhea In line with the widely accepted theory that the corpus luteum exerts a quieting effect upon uterine motility, it seemed logical to employ progesterone, when it became available commercially, in the treatment of functional dysmenorrhea. Since results that followed were no better than those

obtained from diverse other therapeutic agents, it seemed logical to question the occurrence of any specific action. The reason for this therapeutic failure of progesterone seems obvious. Most women with functional dysmenorrhea have no evidence of corpus luteum deficiency, i.e., they bleed from progestational endometria and excrete essentially normal amounts of pregnandiol (a metabolic product of progestin) (6).

Estrogenic bleeding and ovarian sterility
Most of the functional disturbances of menstruation are characterized by estrogenic (anovulatory) bleeding and an associated sterility, i.e., lack of corpus luteum function. It seemed rational to use progesterone in the treatment of these conditions.

Misconceptions occurred at first in regard to the pharmacological effects to be expected from progesterone. It was believed that injections of progesterone would postpone bleeding (i.e., lengthen the interval) when given during nonbleeding phases and that, when given during episodes of excessive bleeding, progesterone would have a hemostatic action. In 1936, we (5) called attention to the fact that the exact contrary was true: progesterone has a hemorrhagic effect when given during nonbleeding phases and increases the amount of bleeding when given during flowing.

Another error in therapeutic theorization was the assumption that a "medical curettage" in these cases, especially in patients with excessively proliferated endometria, could be produced by progesterone by transforming the endometrium to a full blown progestational one which in turn would be shed in the normal fashion. As early as 1936 (5) we cited the infrequent occurrence of progestational responses in these patients following progesterone therapy even when progesterone was synergized with ample estrogens. This phenomenon was related by us to some factor which brought about a lowered endometrial reactivity to progesterone (11).

In regard to the sterility associated with estrogenic bleeding, it seems unlikely that even effective substitution for the absence of progestin would induce ovulation any more readily than in the instances of adolescent ovarian failure wherein substitutional therapy

with estrogens is given. However when estrogens and progesterone are given cyclically as in our regimen of cyclic steroid therapy until normal endometrial reactivity returns a good number of patients experience a return of the fertile state.

Repeated or threatened abortion. Deficient function of the corpus luteum has been predicated to be the etiologic factor in the recurrent or threatening abortions of women in whom no obvious organic or metabolic causes for these abortions exist. Progesterone therapy under these circumstances is founded upon the assumption that these patients need more of the uterine quieting effect of that hormone. Many reports have appeared dealing with the good results obtained from repeated injections of relatively small amounts of progesterone in patients with histories of having had numerous previous abortions.

We have cast doubt recently (8-10) upon the correctness of the premise that corpus luteum deficiency is the cause of the abortions which are prevented presumably when progesterone is administered. Every patient of ours who had critically low pregnandiol (a metabolic product of progesterin) excretions aborted despite intensive therapy with progesterone in amounts many times those commonly used. It is our belief that if progesterone has a specific action in preventing abortions, its *modus operandi* is something other than that of complementing corpus luteum deficits.

USE OF ANDROGENS

Androgens are not considered usually to be "female sex" hormones but a brief discussion of these in this paper seems advisable. It is justified upon two grounds: (1) the fact that these hormones form a part of the normal hormonal pattern of woman and (2) the fact that during recent years there has been a widespread use of androgens in gynecologic therapy.

No clear-cut rationale has been established for the therapeutic use of these steroids in woman (7). The only justification for their use has been apparently that they have pharmacological reactions which under certain circumstances appear to be expeditious, i.e. suppression of ovulation, hemostasis in menor-

rhagia, pituitary stabilization in the climacteric without endometrial stimulation, suppression of lactation, etc.

All of the described effects of androgens have been due to the "negation or overriding of the usual ovarian function" i.e., are contraphysiological effects (4-12). Few if any of the ultimate results obtained by androgens cannot be accomplished more satisfactorily from measures less likely to cause undesired side effects. The use of androgens in the female is beset with the dangers of grave symptoms of virilization not all of which are reversed when therapy is discontinued. One theoretical indication for androgenic therapy is to antagonize hyperestrogenism. The only true and proved instance of this which we know clinically is that which is due to granulosa cell tumors of the ovaries, for which the recognized and satisfactory treatment is surgical ablation of the tumor.

SUMMARY

Estrogenic hormones have a limited, but well established role in the treatment of certain climacteric syndromes, gonorrheal vaginitis of childhood and senile vaginitis. Complementary therapy with estrogens and progesterone in certain instances of intercurrent ovarian failure may be followed by the return of normal ovarian function. Substitutional therapy in severe estrogenic failure of the adolescent or young woman yields only temporary results and does not circumvent the sterility of these patients. Untoward responses to estrogenic therapy are increasing since the availability of cheap orally active estrogens of the diethylstilbestrol type; these are due chiefly to overdosage. Diligence to avoid overtreatment should be observed.

Despite the expectations aroused by the commercial availability of progesterone no definitely established therapeutic role has been accorded it. As a part of cyclic steroid complementary therapy in estrogenic bleeding, it has given best account of itself. Its specific value in dysmenorrhea and repeated or threatened abortion is questioned.

Androgens have no place in rational gynecologic therapy. Their effects are solely of ovarian negating or depressing type. Viril-

ing effects from the use of androgens do not always disappear when the treatments are discontinued

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VISUAL FIELD CHANGES AND SUBDURAL HEMATOMAS

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IT is universally agreed that the clinical diagnosis of subdural hematoma is extremely difficult. Many authorities stress the importance of making exploratory burr holes when the diagnosis is in doubt. A negative burr hole is much less serious than a neglected subdural hematoma. In an effort to improve our diagnostic acumen in respect to this condition we have recently reviewed the series of verified subdural hematomas seen on the neurosurgical service of the Cincinnati General Hospital since October 1937. In the course of this review we were surprised to find that in slightly more than 10 per cent of the cases some mention of a visual field defect was recorded. Knowing the difficulty in examining visual fields, even roughly, in unco-operative patients this percentage seemed remarkable. It therefore seemed probable that a brief review of the type of visual defect, the diagnostic and prognostic value of such defects, and the underlying pathological changes behind the defects might be worthy of brief consideration.

In a series of 63 verified subdural hematomas there were 7 instances in which visual field defects were mentioned (Table 1). In 4 instances these were apparently a very definite finding borne out by careful confrontation tests. In 3 instances the defect was said to be probable. In 1 of the 4 definite examples it was possible to check the fields by actual careful perimetry. In all the cases the defect was homonymous in character. The homonymous defect was contralateral to the hematoma in 4 instances. In 1 case the clot was centrally placed that is interhemispherical, and the defect was a left homonymous abnormality and in the seventh case the visual field change was ipsilateral. Five of the patients recovered and were discharged from the hospital. In 4 of these postoperative checks of the visual fields

revealed no definite abnormalities. In the fifth case that recovered the preoperative homonymous defect had been very definite. A postoperative check 2 weeks after surgery showed a residual almost complete left homonymous defect. This was checked again 1 month after the operative procedure and there was definite evidence of recovery. A third perimetric study was done approximately 2 months after the removal of the subdural hematoma, and at this time the fields continued to show improvement (Fig. 1).

Pathological studies were carried out on the brains of the 3 patients who died. In both cases there was definite evidence of herniation of the uncus portion of the hippocampal gyrus. In both, the greater herniation was in the right side. The clinical evidence in each instance had pointed to a left homonymous visual field defect. In the examination of both brains there was a suggestion that circulation in the posterior cerebral artery on the right had been interfered with by the uncus herniation. The first fatal case (No. 4) was the one in which the hematoma had been interhemispherical. There was gross evidence of moderate softening in the distribution of the right posterior cerebral artery. However in the second case (No. 7) there was very definite gross and microscopic evidence of bilateral posterior cerebral artery involvement with encephalomalacia. This change was much more extensive on the right, the side on which the

TABLE 1.—SUMMARY OF CASES REPORTED WITH EMPHASIS ON VISUAL FIELD AND PUPILARY CHANGES

No.	Side of clot	Visual field change	Pupillary changes	Mortality
1	Left	Right homonymous	Right > Left	Recovered
2	Right	Left homonymous	Right > Left	Recovered
3	Left	Right homonymous	Left > Right	Recovered
4	Central	Left homonymous	Left > Right	Dead
5	Right	Left homonymous	Right > Left	Recovered
6	Left	Left homonymous	Right > Left	Recovered
7	Right	Left homonymous	Right > Left	Dead

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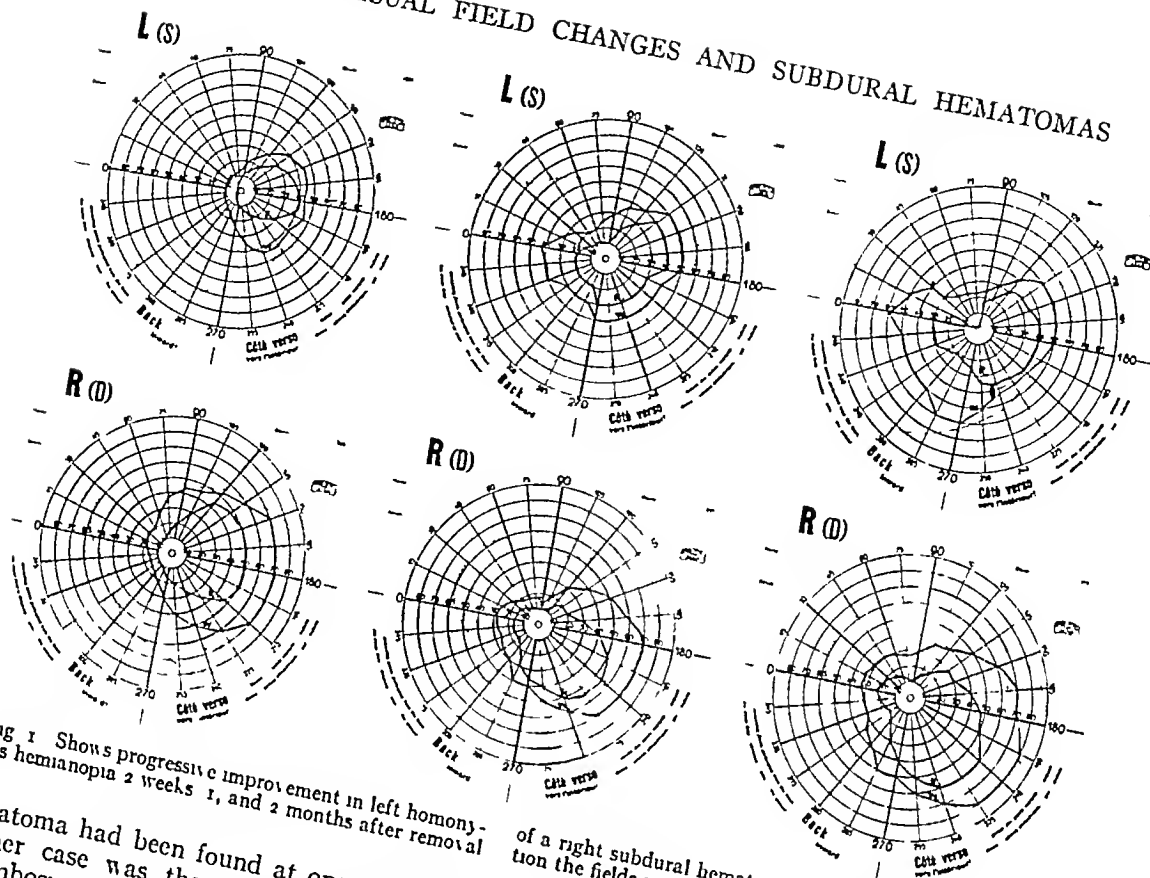


Fig 1 Shows progressive improvement in left homonymous hemianopia 2 weeks, 1, and 2 months after removal of a right subdural hematoma. Because of poor co-operation the fields are not entirely congruous.

hematoma had been found at operation. In neither case was there evidence of actual thrombosis or complete occlusion of the posterior cerebral arteries.

The mechanism of the tentorial pressure cone or uncus herniation is no new concept. The manner in which this change may produce various types of false localizing signs has been discussed by Jefferson, by Kernohan and Woltman, and by Moore and Stern. More recently Schwarz and Rosner as well as Allison and Morison have published complete reviews of the pathological mechanism of embarrasment of circulation in the posterior cerebral artery with tentorial herniation. Reid and Cone were able to produce experimentally certain parts of the tentorial pressure cone syndrome more particularly the pupillary changes. However, it is interesting to note in reviewing the cases reported by these various authors that none mentioned uncus herniation accompanying subdural hematomas. It also would appear that little has been

written about the reversibility of the changes that may occur. We believe that the visual field changes found in this series of subdural hematomas were most probably caused by embarrasment of the circulation in the posterior cerebral artery. Pressure from a herniated hippocampal uncus brought about slowing of the circulation and resulting anoxia in the occipital distribution of the posterior cerebral artery. It is fair to postulate that this change may be of any degree ranging from slight anoxia with transient functional impairment, through anoxia of such severe degree as to cause permanent functional impairment based on profound structural change, a mechanism discussed by Evans and McEachern. This supposition seems to fit the clinical and pathological facts found in this group of cases. It seems probable that in the patients that survived without residuals the factors causing the homonymous defect were mild and reversible. The patient who was followed for 2 months but still showed

slight visual field defects represented more severe tissue damage. Finally the cases which came to postmortem examination represented examples of gross irreversible cerebral softening.

SUMMARY AND CONCLUSIONS

In reviewing a series of 62 subdural hematomas, 7 cases, 11 per cent, were found to show evidence of visual field defect.

The visual field defect was always homonymous in character. In 5 instances it was contralateral to the clot, one was ipsilateral and in one the field defect was leftsided the subdural clot being centrally placed.

Four patients showed complete recovery without residual visual field defects. In one patient careful checks of the fields were carried out at intervals and gradual improvement was observed.

It is believed that too little stress has been put on the complications caused by uncal herniation in cases of subdural hematomas. Moreover it is felt that the visual field changes discussed in this report were caused by tentorial herniation and embarrassment of the circulation through the posterior cerebral artery.

There seems to be good evidence that these changes may frequently be reversible.

Efforts should always be made to determine the presence or absence of visual field defects in patients suspected of having subdural hematomas. In this small series the visual field changes were twice as reliable as pupillary changes in attempting to lateralize the subdural clot. Like other clinical signs that may indicate uncal herniation visual field changes should emphasize the importance of immediate surgical intervention in order to remove the cause of the herniation. The demonstration herewith of the apparent reversibility of the process emphasizes the importance of early effective removal of the source of the herniation.

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THE PROTECTION OF THE OPERATIVE FIELD WITH AN IMPERMEABLE ADHESIVE SKIN COATING

A Preliminary Report

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ANTISEPSIS in surgery is usually considered to have had its origin with Lister's presentation of carbolic acid as a combatant against postoperative infections. In one of his earliest communications he stated "when it had been shown by the researches of Pasteur that the septic property of the atmosphere depended on minute organisms suspended in it it occurred to me that decomposition in the injured part might be avoided by applying as a dressing some material capable of destroying the life of the floating particles" (18). Using his antiseptic methods in his wards at Glasgow, during the 3 year period ending in 1870, Lister succeeded in reducing the mortality rate in amputations from 45.7 per cent to 15 per cent (19). Since Lister's epochal contribution, asepsis in surgery has become a constant and eagerly sought desideratum. It is now generally realized that infection at operations may arise from several possible sources of contamination: (1) upper respiratory tract, hands, hair, skin, and clothing of the operating personnel, and all individuals entering the operating room, (2) the air of the operating room, (3) the instruments and paraphernalia employed in the operation, and (4) the skin of the patient.

Various attempts have been made to control these sources of contamination, the efficacy of which is dependent to a great extent upon the degree of exactitude in application. In 1928, Sutton quoted the statistics of several authors in which the percentages of postoperative infections ranged from 28 per cent to 6 per cent. A review of more recent articles reveals a decrease in the percentages of infection after clean surgical operations, with an average of approximately 3 to 5 per cent (4, 7, 9, 10, 13-15, 26, 27). Beck, in 1936, stated that the incidence of serious infections in clean surgical wounds has been lowered to 1 per cent and of trivial infections to 5.4 per cent. Of the previously mentioned sources of infection which may be present at operation perhaps the most difficult to control with absolute assurance is the skin of the patient. Hirschfeld stated that the normal skin rarely harbors fewer than 10,000 organisms per square centimeter. The general opinion prevails that no antiseptic yet introduced prevents the skin "Of the many sources of wound infection, all, with the single exception of the skin of the operative field, are under the control of the surgeon if he operates with competent help and in proper surroundings" (39). This is clearly demonstrated by the numerous attempts to develop a method which will produce relative sterilization of the skin of the operative field. Even a cursory perusal of the literature will reveal numerous compounds and solutions which have been offered as antiseptics (1, 2, 5, 6, 10, 13, 17, 21-42). A random selection of reported incidences of sterility following the use of four widely employed antiseptics are as follows: merthiolate, 95.4 per cent, tincture of iodine, 71.7 per cent, mercurochrome, 34 per cent, metaphen 91.1 per cent, and several others grouped together, 65 per cent (5, 16, 24, 28, 34, 36, 38, 41, 42). Each antiseptic has its advocates who make glowing claims for its value and its opponents who caution against its uncritical use or condemn it entirely. Allen and associates ob-

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served that the morbidity rates are not widely divergent even though there are clinical differences between the various antiseptics. Hirschfeld stated that in spite of the different pre-operative preparations, the incidence of wound infection in different clinics varies slightly. Almost as numerous as the antiseptics themselves are the various *in vitro* and *in vivo* experimental tests which have been performed to evaluate the effectiveness of these substances (5 8 13, 21 22 24, 28-30 32 33 36 38 40 41). It is fairly well agreed that antiseptics showing excellent *in vitro* tests may not be at all satisfactory in actual clinical use. Likewise, *in vitro* laboratory ratings may not give an accurate index of the quality of the antiseptic, for as Bass points out, organisms added to the skin are more easily killed than the "basal flora."

Price (31) has shown that there are two types of bacterial flora on the skin: (1) the *transient* flora which is loosely attached and can be removed in a few minutes of scrubbing and (2) the *resident* flora which is tightly attached and is difficult to remove. In certain cases the resident flora may include virulent organisms as a result of prolonged exposure to their source. In addition, the bacteria of the deeper layer of the skin are brought to the surface by perspiration, especially during a lengthy operation and may contaminate the wound because the antiseptic applied at the beginning of operation is no longer effective. Therefore this source of contamination is a constant hazard whose threat increases commensurably with the length of the operation. Since the bacteria cannot be completely removed from the skin during the operation their introduction into the wound may be prevented by sealing the operative field with a sterile impermeable surface. Such a surface film has been produced by the use of mercuric bichloride but unfortunately due to perspiration multiplication of bacteria occurs at an increased rate beneath the film (32 33). Consequently any injury to the film allows the escape of the bacteria into the wound.

The current method of preparing the operative field consists of shaving, careful soap and water scrub, defatting application of an antiseptic agent, and draping of the area with

sterile towels. After the incision is made sterile towels are clamped to the edges to protect the wound from possible skin contamination. It is generally realized, however, that this careful preparation of the skin and the clamping of towels around the wound edges are measures of only relative efficiency and that they do not absolutely protect the wound from such contamination.

Obviously if there could be applied to the skin in the region in which the incision is to be made some impermeable substance which is sterile and which would adhere to the skin, the incision could be made through it and absolute protection from skin contamination would be afforded. Such a covering which would be most efficient should possess the following properties: (1) impermeability to bacteria (2) bactericidal action (3) non-irritancy (4) transparency (5) adhesiveness to skin (6) elasticity and (7) facile incisibility.

Because it fulfilled all these conditions except the first three, vinylite resin¹ was tested for the possibility of fulfilling the other requirements. This resin is a polymerized vinylite acetate which is soluble in practically all common solvents with the exception of water, gasoline and the higher alcohols. It is colorless, odorless, nontoxic, and it resists dilute salt, acid, and alkali solutions. It is widely used as an adhesive for a variety of materials and is an excellent adherent to practically all types of surfaces. It absorbs water and becomes leathery and pliable when large amounts are absorbed (43).

Several preliminary tests were tried in the laboratory before clinical application was begun. Solutions of the resin were made in different percentages to determine the formula which gave a satisfactory coating and which dried most rapidly. On the basis of these studies, the following formula was adopted:

- 5 grams vinylite resin, AYAF
- 50 acetone
- 3 grams nitrocellulose (to hasten drying)

This solution of vinylite resin was applied to the skin of volunteers and allowed to remain intact from 24 hours to over a week. Its

¹This material was supplied through the courtesy of Dr. A. C. Church, of the Carbide and Carbon Chemical Corporation.

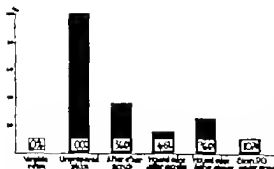
adhesiveness was definitely demonstrated and on peeling off the transparent resin, the skin beneath was dry and unaffected even at the end of a week. Skin irritation was never observed. Fifteen sterility tests were made. One-half cubic centimeter of resin was inoculated into tubes of meat digest broth and incubated aerobically and anaerobically for 4 days at 37 degrees C. At the end of this period, none of the tubes was sufficiently cloudy to justify the notation of positive growth. Therefore, all tubes were streaked on blood agar plates and incubated aerobically and anaerobically for 24 hours at 37 degrees C. Of the 30 plates, only one showed a growth of nonhemolytic *Staphylococcus albus*. An attempt was made to determine the bactericidal power of the solvent, acetone. Increasing dilutions of acetone were made with sterile broth, and these tubes were inoculated separately with *staphylococcus*, *streptococcus*, and *Bacillus coli*. At the end of 24 hours incubation at 37 degrees C, the tubes were replated and failed to show growth on the 1:1 dilution. Dilutions of 1:5 or higher had little or no bacteriostatic effect. Tubes of the prepared resin were inoculated separately with the same 3 organisms and transplants were made to tubes of meat digest broth and blood agar plates at the end of 8 minutes, 15 minutes, and 30 minutes. All tubes were negative and only one colony of *staphylococcus* grew on the plate made at the end of the 8 minute period. Since the real test of the compound is its usefulness clinically, the vinylite resin solution was tried on a series of cases. For this purpose, 1 per cent phenol was added to the formula to enhance its bactericidal powers. It was determined that this produced no changes in the chemical and physical properties of the resin as described above. This vinylite resin solution was used in 30 clean surgical cases. The usual ward preoperative preparation of shaving and soap and water scrub was performed. In the operating room, the area was scrubbed with ether, and painted with vinylite resin by means of a soft rubber applicator, and draped with sterile sheets to limit the operative field. When the sterile drapes were thus applied over the vinylite resin before drying had occurred the sheets would adhere closely to the skin at the borders of the operative field and towel clamps for the purpose of holding the sheets in place are obviated. This is particularly advantageous in areas having curved and irregular surfaces, such as in breast or thyroid operations. When the solution was applied in proper thickness, drying was complete within 5 minutes. The length of time and the type of each operation were noted. Most of the operations consisted of appendectomies, thyroidectomies, cholecystectomies, herniorrhaphies, and phrenectomies, and the duration of the procedures averaged 46 minutes. In each case, 6 groups of bacteriologic studies, depending upon the site of swab cultures, were made as follows: (1) solution of vinylite resin, (2) the skin of the operative field immediately after the patient's entrance into the operating room, (3) skin surface after ether scrub, (4) skin edge immediately before incision, (5) skin edge immediately before closure of incision, and (6) skin surface approximately 3 inches from the wound after the resin was stripped back and before the application of the dressings. The cultures were sent to the laboratory where each was streaked out on two blood agar plates and inoculated into two tubes of meat digest broth, one of each was incubated anaerobically and the other aerobically for 48 hours. At the end of this period, the plates were examined for growth, and the tubes were replated and incubated aerobically and anaerobically for a period of 24 hours.

The results of these bacteriological studies may be briefly summarized as follows.

Group 1. In 27 cases, the bacteriological studies on the solution of vinylite resin immediately before its application to the operative field showed no growth.

Group 2. In 30 cases the bacteriological studies made on the skin of the operative field before it was prepared except by shaving and washing with soap and water showed 100 per cent growth. *Staphylococcus* was recovered most frequently, which is comparable to other reports (11, 12, 14, 15, 26).

Group 3. In 30 cases, these studies on the skin of the operative field immediately after it was prepared by ether scrub showed the presence of growth in 11 (36.6 per cent) cases.



Graph Graphic representation of incidence of positive growth in bacteriological studies on the use of vinylite resin

Group 4. In 30 cases, the bacteriological studies of the skin edge immediately after the skin incision was made showed the presence of organisms in 5 cases or 16.6 per cent. Of these 5 cases 4 were positive in group 3 and showed organisms with similar bacteriological properties.

Group 5. In 30 cases, these studies made on the skin edge at the completion of the operation and before the skin edges were closed showed the presence of organisms in 8 cases or 26.6 per cent. Of these 8 cases only 1 was also positive in groups 3 and 4, and 3 were also positive in group 3 alone.

Group 6. In 28 cases, bacteriological studies made immediately after the completion of the operation on the skin surface in the operative field under the vinylite resin showed the presence of organisms in 3 cases or 10.7 per cent.

EVALUATION

Whereas it is recognized that the results of these bacteriological studies are based upon too few cases to be of conclusive significance they were considered of sufficient interest to be presented as a preliminary report. Moreover it should be realized that these bacteriological studies were done with the purpose of determining whether vinylite resin solution would fulfill the desiderata previously considered in the ideal preparation of the skin of the operative field. The clinical application of this method of skin preparation clearly demonstrated that it fulfilled the requirements of transparency, adhesiveness to the skin, elasticity, ready incisability and non

irritancy. The significance of these requisites of such a skin preparation is clearly apparent. Transparency is desirable because it permits the surgeon to place the incision accurately according to the landmarks which may be clearly seen. The significance of adhesiveness to the skin lies in the fact that unless the impermeable film adheres closely and tenaciously to the skin there is the possibility that during the operative procedure perspiration containing organisms which have escaped from skin pores may readily seep beneath the film toward the edge of the incision. This is likely to be enhanced further by retraction and manipulation during the operative procedure. For this reason, the film must possess an elastic quality somewhat comparable to the skin to which it adheres. It was found that the vinylite resin film was readily elastic and simultaneously stretched with the skin and remained definitely adherent to it as the wound was retracted and manipulated. In fact it was observed that this adhesive and elastic quality remained present for several days after the operation. Moreover skin irritation was never observed in any of the cases even after the film had been allowed to remain in contact with the skin for as long as one week. In a few cases the vinylite resin solution was applied to the irritated skin surrounding an enterostomy opening and it was found to have a definitely protective and beneficial effect. Obviously this is another purpose for which it may be used to great advantage.

The results of the bacteriological studies clearly demonstrated its bactericidal activity. Bacterial growth was obtained in none of the 27 cases in which these studies were made on the solution itself (Graph 1). This is particularly significant in view of the fact that no special attempt was made to sterilize the solution. Moreover the solution was readily exposed to contamination since the rubber applicator was repeatedly dipped into the solution after it had been applied to the skin of consecutive patients.

The fact that bacteriological growth was obtained from the skin of the operative field in all of the cases after it had been prepared by shaving and washing with soap and water is to be expected and conforms with similar

previous studies (8, 22, 24, 31) It merely emphasizes further the importance of careful and more effective methods of preparing the skin of the operative field Of particular interest is the fact that bacterial growth was obtained from the skin after ether scrub in 36.6 per cent This would seem to indicate that ether has a sterilizing ability of over 60 per cent, but this is not in accord with other studies (20, 32, 34, 36) Price (32) has expressed the opinion that ether is valueless as a sterilizing agent of the skin However, its detergent qualities are generally recognized and for this reason it is considered of definite value in the preparation of the operative field Perhaps the unusually low incidence of bacterial growth after ether scrub in this series may be explained by the fact that this was performed with especial vigor and thorough care, 8 or 9 separate scrubbings being used In our opinion this is significant and demonstrates the value of such careful mechanical cleansing

The results of the bacteriological studies of the skin incision edges immediately after the incision was made and following the completion of the operation immediately before the incision was closed are also of interest The fact that bacterial growth was obtained in only 16.6 per cent of the cases in the former instance and that this incidence had risen only 10 per cent in the latter would seem to indicate the effectiveness of this method of preparation Somewhat comparable studies were made by Maddock and Georg (22), who found an average incidence of contamination (with the use of mercuric iodine, merthiolate, and 2 per cent iodine-and-50 per cent propanol) of 37 per cent at the beginning of the operation and 60 per cent at the end of the operation, an increase of 23 per cent Certainly if contamination is given other factors which may act as sources of contamination in increasing this incidence such as the air of the operating room and the manipulation of the wound with consequent squeezing out of bacteria at the skin edges the possibility that the skin of the operative field as a source of contamination in increasing this incidence would seem to have been reduced considerably This would indicate further that the vinylite resin film is

effective as regards impermeability This is also supported by the fact that all of the wounds healed by primary union and in none was there any evidence of even trivial infection

Perhaps one of the most significant findings in this connection is the fact that at the completion of the operation, bacterial growth was obtained from the skin of the operative field after peeling off the vinylite resin film in only 10.7 per cent of the cases It must be admitted that this was an unexpected observation Certainly if bacterial growth was obtained from this skin in 36.6 per cent of the cases before the film was applied, one would expect a higher incidence three-quarters of an hour later during which the factors of perspiration and manipulation of the skin with consequent escape of organisms may have been operative The explanation for this unexpected decrease in bacterial growth probably lies in the observation that the skin was absolutely dry when the vinylite resin film was peeled away This may be due to the operation of several factors, the significance of which can be only speculative Perhaps the vinylite resin produces a local inhibitive influence on perspiration or it may have an absorptive action Whatever the explanation may be, of practical importance is the fact that it has a desirable and bacteriostatic effect

SUMMARY

- 1 A brief discussion is presented of the importance of a sterile operative field Two types of bacterial flora are present on the skin (1) the transient which is easily removed by a few minutes scrubbing, and (2) the resident which is very difficult to remove
- 2 An ideal covering for the operative field should possess the following qualities (1) impermeability to bacteria, (2) bactericidal action, (3) nonirritancy, (4) transparency, (5) adhesiveness to skin, (6) elasticity, and (7) facile incisability
- 3 Vinylite resin fulfilled the requirements in laboratory tests, and was employed successfully in 30 clean surgical cases
- 4 Further studies are being carried out at the present time to substantiate its value for this purpose

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PERITONEOSCOPY

New Applications and a New Supplementary Instrument

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THE peritoneoscope, devised for visualizing the abdominal cavity and its viscera, is similar to the foreoblique cystoscope except that it is larger and uses an air medium, whereas the cystoscope uses water. After preliminary pneumoperitoneum, the sheath and trocar tip are introduced into the abdominal cavity through a small stab wound. The trocar is then removed, the peritoneoscope inserted and an examination made. Biopsies can be taken with a special forceps which carries a small observation telescope. A detailed description of peritoneoscopic technique has been made by Ruddock (9, 10) who, in 1934, devised the instrument now most widely used. This author's last 750 cases without a single mortality testify to the safety of the procedure. Carried out as it is under local anesthesia, it is, furthermore, a minimal operation. As a rule, the patient may be up and around 8 hours after an examination, or the following day if a biopsy has been taken.

I wish to describe a new instrument for assisting peritoneoscopy and to present from my series of 125 cases several new or little exploited applications of peritoneoscopy.

THE NEW INSTRUMENT¹

The new instrument consists of a blunt tipped rod or "manipulator" and an insulated endothermy electrode, both of which fit into the sheath of a small paracentesis trocar through an airtight rubber nipple (Fig. 1).

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Presented in the Forum on Fundamental Surgical Problems before the Clinical Congress of the American College of Surgeons, Boston, November 3-7, 1941.

¹This instrument was presented both in an exhibit and in a moving picture at the meeting of the Southern Medical Association in Louisville, November 15-19, 1940. The diathermy electrode was added 3 or 4 months later. Two other authors in recent publications have independently described instruments auxiliary to peritoneoscopy. Robinson and Fisk use an instrument similar in principle to our own and Lamb described a transparent bladder that can be inflated around the peritoneoscope, thus pushing viscera aside.

When needed, the trocar and sheath are introduced through a tiny separate stab wound. Under peritoneoscopic view, the trocar is removed and the manipulating rod or electrode is inserted. The electrode is capable of dividing adhesions, opening benign cysts, etc. With the rod, obstructions to peritoneoscopic vision are pushed aside or hidden structures lifted into view (Fig. 2). The liver and gall bladder, usually accessible to the peritoneoscope, may either one or both become obscured by adhesions or loops of bowel. These obstructions can be gently pushed one way or another to allow adequate visualization. When overlapping, the edge of the liver can be lifted up to disclose the gall bladder, hidden between it and the colon. The spleen, not often seen by the unaided scope, unless greatly enlarged, can usually be manipulated into view. The appendix almost always hidden by loops of ileum or by the cecum, is easily lifted up for inspection by the rod. In the pelvis, tubes and ovaries are sometimes partly or completely hidden by their prolapsed position, but the tip of the instrument hooked under the round ligament will pull them up into plain view. Sigmoid, cecum, and colon can be pushed about to secure the best visualization.

We have so far used the auxiliary instrument 31 times. There have been no accidents and the results have been gratifying.

NEW APPLICATIONS OF PERITONEOSCOPY

Knowing the potentialities of the peritoneoscope and accessory instrument, the trained peritoneoscopist will come to adapt it to a widening variety of diagnostic and therapeutic problems outside its recognized routine. The following are examples.

Gunshot and stab wounds of the abdomen of doubtful penetration. Heretofore, surgical exploration has been the accepted means of ruling in or out perforation of the parietal

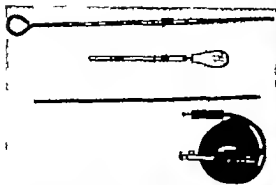


Fig. 2. The new instrument consisting of small trocar and sheath, manipulating rod, carrying the airtight rubber nipple and the insulated endothermy electrode and cord.

peritoneum. Pentoneoscopy will give the same information, for by probing the debrided entry wound with a hemostat the suspected area of peritoneum is tented forward for inspection through the pentoneoscope (4).

Prior to our use of the pentoneoscope in these cases, 12 per cent of all surgical explorations of abdominal bullet and knife wounds at the Louisville City Hospital revealed no penetration and hence were unnecessary. Furthermore, well over 90 per cent of these wounds were so located that their penetration or nonpenetration could be reliably determined by means of the pentoneoscope. So far pentoneoscopy was done in 16 patients with such injuries. In 7 of these penetration was found, thereby indicating immediate laparotomy. The other 9 patients were spared a laparotomy by visualizing an intact parietal peritoneum beneath the entry wound.

Differentiating between appendicitis and salpingitis and between appendicitis and cholecystitis. All are familiar with the occasional female patient who is suspected of having salpingitis but upon whom an exploratory operation is performed to rule out an acute appendicitis. In these cases it is our practice first to inspect the adnexae. If they cannot be visualized by the unaided pentoneoscope they are easily hooked up for inspection by the manipulator. If salpingitis is found for confirmation the appendix is lifted up on the rod and examined for abnormality. If the



Fig. 3. The manipulating rod in use.

tubes are normal and the appendix appears suspicious, laparotomy is performed.

So far we have used the pentoneoscope in this differential problem 5 times with complete success and with no untoward results. Three times a diagnosis of salpingitis was made and laparotomy avoided, and once the diagnosis of appendicitis was made and verified at operation. Once early appendiceal peritonitis was unexpectedly discovered. The patient was treated conservatively by the Ochsner regimen and made an uneventful recovery. Interval appendectomy 5 months later confirmed the previous diagnosis and revealed normal adnexae.

Rarely a differential problem arises between acute cholecystitis and acute appendicitis. This was exemplified recently on our wards by a 22 year old negro male. Symptoms and signs pointed chiefly to early acute cholecystitis, but an inflamed high lying appendix could not be ruled out. Pentoneoscopy was performed and by this means a distended, injected gall bladder was visualized. Pressure against it through the abdominal wall caused pain. The appendix was then lifted up by the manipulator and found to be normal. The patient's symptoms subsided satisfactorily on a conservative regimen.

Lysis of adhesions and rupture of ovarian cysts

Benedict and others have aspirated ovarian cysts under peritoneoscopic guidance. The only case we could find of peritoneoscopic lysis of intra-abdominal adhesions was reported by Jones in which he divided bands between liver and diaphragm to allow more complete pneumothorax. Since devising the insulated endotherm electrode a year ago, we have encountered only 1 patient suffering from genuine painful adhesions. This was a 44 year old negroess with persistent sticking pain beneath the right breast of almost incapacitating severity. Roentgen studies of the chest, gall bladder, and gastrointestinal tract were negative. Peritoneoscopy revealed a normal gall bladder, old pelvic inflammatory disease, and Curtis' "violin string" adhesions between the liver and the anterior abdominal wall and diaphragm. Tugging on these exactly reproduced the sticking pain. The adhesions were divided with the cutting electrode under peritoneoscopic guidance and after 6 months the pain has practically gone and the patient has returned to work.

On 2 occasions we undertook to rupture follicular cysts of the ovary in young women with severe menorrhagia who had not responded to hormone therapy. The purpose was to remove, if possible, the stimulus for the excessive flow. In 1 patient examined before we had devised our manipulating rod, we were unable properly to visualize the ovaries. At laparotomy subsequently a cyst of the right ovary was found. In the second patient a follicular cyst of the left ovary was found and punctured with the escape of about 2 ounces of straw colored fluid. For 6 months the patient's excessive flow gave place to occasional scant bleeding or spotting and the endometrial biopsy changed from hyperplasia to anovulatory hypoplasia. The patient was so well pleased that when flooding recommenced, she requested another peritoneoscopy. However, the second examination revealed only small sclerosed ovaries and no sign of the previous cyst. The patient is now being given a trial of lactogenic hormone before surgery is resorted to.

Nonpenetrating abdominal trauma when internal injury is suspected Ruddock (10) and

Fry both recommend endoscopy. Nevertheless, we feel that the findings in cases of nonpenetrating abdominal trauma when internal injury is suspected must be interpreted with caution. Peritoneoscopy can safely rule in or out rupture of spleen or liver. However, although the discovery of laceration of bowel or stomach would constitute a clear-cut indication for surgery, the failure to find hollow viscerai injury by the peritoneoscope would by no means rule it out.

Peritoneoscopy was performed in the case of 1 boy whose abdominal findings were only mildly suggestive of intraperitoneal hemorrhage following a bicycle accident. The discovery of moderate hemoperitoneum decided us upon surgery. At operation 2 lacerations in the right lobe of the liver were found and repaired. The boy made an uneventful recovery.

Differentiation between bleeding peptic ulcer and ruptured esophageal varix About 2 years ago we had the embarrassing experience, upon operating for massively bleeding peptic ulcer, of finding instead a typical hobnail cirrhotic liver and, indirectly, bleeding esophageal varices. A few months later we met with a somewhat similar case. This time, though ruptured varix seemed more likely, there were no ascites and bleeding ulcer could not be ruled out. A peritoneoscopic examination was gently performed, revealing a typically cirrhotic liver and thereby removing any question of surgery. It seems that this procedure is less likely to restart or to aggravate bleeding and is more certain in diagnosis than the alternative barium swallow proposed by Schatzki.

SUMMARY AND CONCLUSIONS

We have presented a new instrument to assist peritoneoscopy and have described a few new applications of the procedure to surgical problems with the same purpose in each case, that of avoiding laparotomy.

A number of authors (1, 8) warn against peritoneoscopy in cases of suspected penetrating abdominal injuries and the vast majority give as a contraindication any suspected acute inflammatory condition, such as acute appendicitis or salpingitis. However, in those cases in which exploratory laparotomy is the

only alternative method of deciding whether or not surgery is indicated and in which peritoneoscopy is equally capable of making that decision. I urge that peritoneoscopy be chosen on the grounds that it is much the lesser and safer procedure seldom incapacitating the patient for more than 24 hours.

Incidentally 3 of our 4 accidents (bile fistula from liver biopsy in a case of obstructive jaundice moderate hemorrhage following splenic biopsy in a case of monocytic leucemia, and perforation of ileum in a far advanced case of fibrocaceous tuberculous peritonitis) occurred in generally accepted and what we might term medical applications of peritoneoscopy. The only untoward result among

the "surgical" uses of the instrument was a mild pneumothorax caused in a patient with gunshot wound of the abdomen in which the bullet also penetrated the diaphragm.

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positive tests for protein. Solutions containing 1 milligram per cubic centimeter are opalescent and milk like. The results of elementary analysis and fractionation given in a succeeding paragraph show the material to be nucleoprotein containing possibly a very small amount of fat.

HOMOGENEITY AND PHYSICAL STATE OF THE PROTEIN

The problem for first consideration has been the determination of the degree of the purity and homogeneity of the isolated protein in order to establish a basis for evaluating the results of analyses on constitution and behavior. Recent advances in the study of proteins have provided a number of physical tests suitable for application to this problem. Those used singly or in combination have been studies on (a) homogeneity with respect to rate of sedimentation in the analytical ultracentrifuge (b) homogeneity of electric charge density as measured by the reversible spread of the moving boundary in the Tiselius electrophoresis apparatus (c) the rate and manner of diffusion and (d) the viscosity of the purified protein solutions.

Sedimentation velocity studies in the analytical ultracentrifuge give information based chiefly on particle shape, size and mass. Such studies were made in parallel with development of the procedures of isolation. Examination of solutions of pellets obtained in the initial sedimentation in the quantity ultracentrifuge revealed the presence of an ultraviolet light absorbing material with a sedimentation constant of about $S_{20} = \text{ca. } 250 \times 10^{-13} \text{ cm. sec.}^{-1} \text{ dynes}^{-1}$ (1). In such a preparation the sedimenting boundary was not entirely sharp and there was seen also some of the usual tissue protein of molecular size so small that no sedimentation of it occurred in the ultracentrifugal field employed in the study. After 3 to 5 cycles of low and high speed spinning however there could be seen only the specific material all light tissue protein and very heavy insoluble colloidal material having been eliminated. With such a product the sedimenting boundary was very sharp and from studies of many samples, the sedimentation constant was $S_{20} = 278 \times 10^{-13} \text{ cm.}$

$\text{sec.}^{-1} \text{ dynes}^{-1}$ (8). The sharpness of boundary and freedom of products other than those associated with the specific boundary demonstrate a very high degree of homogeneity of the purified material with respect to this method of study. The examination of other substances by this method has shown that such a degree of homogeneity has been evident only with solutions of a single molecular species. These results, together with the high sedimentation constant, indicate the purified material to be a high molecular weight protein.

Further information of the physical nature and state can be obtained by examination in the Tiselius apparatus. For this purpose solutions containing 2.7 to 4.5 milligrams purified protein per cubic centimeter were studied (11) in the pH region from 3.78 to 7.7 the range in which the material is stable (2). In periods of 54 to 23 hours, the protein particles migrated with a single very sharp boundary. The symmetry and singleness of boundary and its sharpness or lack of spread revealed a degree of electrophoretic homogeneity which has been seen only with solutions of a few highly purified proteins. These results indicate a remarkable similarity in electrical properties amongst the individual protein particles and thus provide a second and strong indication for the molecular state of the protein.

Evidence for the monodispersity of the protein has been seen in diffusion experiments. The rate of diffusion is a function of the size and shape of the protein particles. The shape of the diffusion curves is dependent on the degree of homogeneity. The experimental curves (8) observed here were of the shape of a gaussian normal error curve, revealing an ideal diffusion behavior and thus high uniformity in the size and shape of the particles. The observed low diffusion constant, $D_{20} = 6.65 \times 10^{-8}$ was again indicative of large molecular size.

The relative viscosity of a protein solution is a function of particle shape and practically independent of particle size. Studies on solutions of the purified protein showed that the relative viscosity was a linear function of protein concentration. This result is indicative only of normal flow and alone is not an index of the state of dispersion. On the other hand,

the shape factor evaluated from viscosity data agreed with that calculated independently from the sedimentation and diffusion data. In the face of this agreement, the viscosity results can be considered additional evidence of homogeneity.

The results of sedimentation, electrophoresis, and diffusion experiments furnished evidence of a degree of monodispersity of the purified protein equal to that of the most homogeneous proteins studied. From a combination of diffusion with sedimentation and viscosity data, the shape of the molecule is seen to be that of an oblate ellipsoid with an axial ratio of 1:1 if hydration is neglected. The density of the material is 1.323, which together with sedimentation and diffusion data gives a value of 47,100,000 for the molecular weight.

RELATION OF THE PROTEIN TO THE PAPILLOMA VIRUS

These investigations have served, within the limits of the methods, to demonstrate the high state of purity of the isolated product and its existence in the molecular state. These tests are based on physical and chemical properties of the protein and serve to show that only one material is present. The problem now becomes that of determining the relation between this purified protein and the virus. The causative agent of the growth is recognizable only by its biological behavior, and a correlation of the properties of the protein with those of the virus can be accomplished solely through biological response in animal experiments. Because of the recognized variation in animal work, the results of biological tests cannot be employed as estimates of physical and chemical homogeneity but can be utilized for judgment of uniformity of behavior. Any correlation of the properties of the protein with those of the virus is dependent finally on the limits of the biological method employed.

The chief biological property of the virus is infectivity or the capacity to induce lesions in the form of warts. It has consistently been found that infectivity is associated with the protein. In numerous experiments, the yield of purified material has been roughly propor-

tional to the infectiousness of the wart extracts from which it was derived. This is strikingly emphasized in comparing results of ultracentrifuging cottontail rabbit warts with those of similar procedures on domestic rabbit growths. Naturally occurring warts from most cottontail rabbits are usually highly infectious. On the other hand, infectivity is rarely seen with extracts of domestic rabbit growths. Despite ultracentrifugation of many liters of extracts of domestic rabbit growths, no high molecular weight protein has been seen.

For studies on specific infectiousness associated with the purified protein, a special method has been developed (3) for its measurement with a relatively high degree of expected accuracy. Employing nitrogen content as an index of protein quantity, there has been found a linear relationship between the logarithm of protein amount and the incubation period in days of warts induced with it. With this procedure, many samples of the protein have been found highly uniform in their degree of infectivity. The infectious unit of protein, in terms of that quantity of it required to produce lesions at 50 per cent of the spots inoculated, is $10^{-8.305}$ grams (4). As a routine procedure, the volume of inocula has been 0.1 cubic centimeter of protein solution. From the molecular weight it has been calculated that this infectious unit is comprised of an average of 56,800,000 molecules in 0.1 cubic centimeter of inoculum. The uniformity of behavior is shown in the results seen with several different batches of material which have given infectious units of $10^{-8.355}$, $10^{-8.285}$, $10^{-8.3}$, and $10^{-8.368}$ grams. These findings, as determinations of virus infectivity, are in exceedingly close agreement. Another biological method used was complement fixation which gave results (6) of uniformity paralleling those with infectivity. Perhaps the most satisfying demonstration of uniformity is the quantitative nature of the serum-protein relations in the neutralization reaction (5). The constancy of the results is such that the reaction can be expressed mathematically with high accuracy.

Further evidence is available of close relationship between the protein and the papil-

loma virus. This is especially illustrated in parallel studies (2) on molecular stability of the protein and virus infectivity with respect to hydrogen ion concentration. Molecular stability is at a maximum between pH 2.9 and 10. This is likewise the region of maximum stability of virus infectivity. In solutions more acid than pH 2.9, the molecules disintegrate, as shown by analytical ultracentrifugation and here infectivity is lost immediately. In the alkaline range however infectivity is immediately lost at pH 10 where as molecular disintegration begins quickly only at pH 10.3 or above. The isoelectric point of the protein is at pH 5.0 where the protein is insoluble. Here the protein precipitates, and with it are carried the infectious qualities of the solution.

The foregoing results serve to establish with reasonable certainty the identity of the purified papilloma protein and the papilloma virus. The experimental findings thus can be interpreted as describing the properties of this infectious agent. Elementary analyses (1) have shown the virus protein to contain carbon, 49.6 hydrogen 7.2 phosphorus, 0.94 nitrogen 15.0 and sulfur 0.22 per cent. There is present 6.45 per cent carbohydrate. The possibility of fat as a conjugated constituent is still not entirely clear. Early fractionation with small amounts of material gave 3.1 per cent lipid. More recent investigation (18) has indicated a value of 1.49 per cent. Fractionation (18) has revealed the presence of nucleic acid to the extent of about 8.0 per cent. The nucleic acid is definitely of the thymus type there being no detectable trace of ribose or yeast nucleic acid.

EVALUATION OF STUDY

In the experiments described, a specific material exhibiting the biological characters of the rabbit papilloma virus has been isolated from infectious extracts of growths from cottontail rabbits. This component of the growths fulfills the criteria of a homogeneous macromolecular nucleoprotein which may or may not contain a small quantity of conjugated fat. The evidence thus far obtained indicates that this macromolecular material is the papilloma virus.

For present interpretations, the results of these investigations of the causative agent of the rabbit papilloma are best considered in comparison with the findings on other filterable viruses rather than other tumor agents. During the past few years, much attention has been given to studies on the isolation and properties of viruses, both those causing disease in plants and those pathogenic to animals. In 1935 Stanley (15) announced the isolation of a high molecular weight protein from plants diseased with tobacco mosaic virus. This material obtained by classical methods of chemical fractionation is crystalline, and its identity with the virus of tobacco mosaic disease has been well established. Subsequently with access to the newly developed air-driven ultracentrifuge numerous other plant virus proteins (16) have been isolated, and all thus far studied possess properties ascribable to entities existing in the molecular state rather than those to be expected of individuals classed as bacteria. Similar studies in the field of animal viruses have proceeded much more slowly. It has been possible to concentrate and to purify to a considerable degree a number of these agents. Only a few have been procured in amounts and in a state suitable for study namely the elementary bodies of vaccinia (7) the rabbit papilloma virus and the agent of equine encephalomyelitis (12). The criteria for judging the nature of these 3 viruses, however are not applicable to the same extent for each of the three. Chemical analyses of vaccinia elementary bodies have given fairly uniform results. Microscopic examination has been employed for interpretation of homogeneity of purified preparations, but the findings can hardly be considered quantitative and further provide no indication of the nature of the bodies. Numerous studies have been made on the bodies in the analytical ultracentrifuge and those workers (14) having the widest experience have reported spread in the sedimenting boundaries indicating lack of uniformity in particle size. The elementary bodies are not of a nature suitable for electrophoresis studies by the moving boundary method (14) and other tests have not been applied. The results as reported cannot be employed to place the

elementary bodies definitely in either the category of molecular or that of bacterial entities. Considerably better evidence is at hand of the nature of the equine encephalomyelitis virus. Sedimentation diagrams (17) of the purified material show the sharp boundary of molecular substances. None of the data thus far obtained are incompatible with the view that this virus also is molecular.

In striking contrast to the findings with these other animal viruses are those with the papilloma virus protein. Here many of the rigid criteria of the physical state of proteins in general are applicable, and in all instances the results have consistently demonstrated the homogeneity and the molecular nature of the protein. The papilloma protein is thus at least one animal virus which can be grouped with assurance with the macromolecular plant virus nucleoproteins.

SUMMARY

The isolation and properties of a specific material from virus-induced cottontail rabbit papillomas have been described. This material, which behaves biologically as the virus responsible for the disease, is a nucleoprotein obtainable in solutions of high homogeneity. Its physical properties with respect to sedimentation, electrophoresis, diffusion, and viscosity are those of a molecular substance.

The values obtained in such studies indicate a molecular weight of 47,100,000. With respect to the physical state, this animal virus falls into the same category as occupied by the macromolecular plant virus nucleoproteins.

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THE GENERAL SURGEON'S APPROACH TO THE PROBLEMS PRESENTED BY FRACTURES AND OTHER TRAUMAS

WALTER ESTELL LEE, MD F.A.C.S., Philadelphia, Pennsylvania

PROBABLY many question the need for a discussion of a subject which seems to have been settled for some time by the orthopedists and the patients. In urban, most suburban and even in the rural districts, the patients themselves are consulting the orthopedists directly for the treatment of fractures, thus short circuiting the traditional route via the general practitioner the general surgeon while, for the correction of resulting permanent deformities, the orthopedist has a clear field.

This is a general statement, and the practice varies in different parts of the United States and Canada, but it would seem fair to say that it is only in the older parts of our land in the regions where one finds the litter of antiques and traditions persisting the general surgeon still has the undisputed privilege of treating fractures. If this is the trend of the times is it right or wrong and if wrong what should or could be done about it by the general surgeon?

Is the specialization of surgery rational necessary or in the best interests of the patient? I feel sure we are on common ground when claiming that irrespective of our personal interests it will be the welfare of the individual patient which will and should govern the practice of medicine and surgery in the future.

Some years ago I discussed this subject with Dr. Meeker then dean of the Graduate School of Medicine of the University of Pennsylvania, and from what I have already said you will understand my side of the argument. I was not convincing him by any means, and finally a little heatedly I asked if he would define a specialist. He quickly and positively replied as he usually does, "a specialist is a surgeon or an internist who can and does one

thing well, and does it better than any one else." Again upon my request for his definition of a general surgeon his answer came just as promptly as before a general surgeon is one who does not do any one thing particularly well.

The passing of time has softened to some extent my immediate resentment so much so that I am offering his definition as a text for our consideration.

You will note that Dr. Meeker said *does not do any one thing particularly well* But he did not say "cannot." This seems to me to open the way for our discussion.

Is it true that the lay public (for Dr. Meeker is not a doctor of medicine but a doctor of philosophy in biochemistry) agree that general surgeons do not do any one thing particularly well and if so why? Is this attitude toward fractures much different from that which they have toward other specialties including obstetrics and gynecology genitourinary surgery neurosurgery facial maxillary surgery plastic thoracic and one of the latest diseases of the peripheral vascular systems?

In many of the medical schools at the present time all these fields of surgery are being taught by specialists, not by the general surgeons and is it any wonder that the graduate medical student when he becomes a practitioner refers his traumatic surgery, or at least his fractures, to the orthopedist? This being so and if the orthopedist does not give as good service to the patient as the general surgeon will this practice continue for long? I doubt it, for sooner or later the patient, or his family doctor will properly evaluate the services received.

By this indirect approach we come to the crux of the situation, as expressed by Dr. Meeker. Does the general surgeon give to the fracture patient as good or better service than the orthopedist? I shall deliberately avoid

giving my answer to that question for the time being

The next question then *can* he provide, as a result of his training and experience in general surgery, as good or better service than the orthopedist? I am positive that he can and should

My thesis, then, is that the general surgeon, because of his broad surgical training, should be able to compete successfully with the orthopedist in the care of trauma of the soft tissues, bones, and joints, but I have a feeling that he is not holding his own at the present time

Recently a new specialty has been developing, that of traumatic surgery, composed of general surgeons who are interested in fractures, and orthopedists who are interested in the general problems of trauma. This may be the answer to the dilemma, for in such a group we find surgeons who are particularly interested in the treatment of traumatic conditions, and orthopedists who are willing to admit that they need a much broader training in the care of trauma than is provided by a limited experience in the regional field of bones and joints. It may be that the surgeons of South America have already solved this quandary, for during a recent conversation with Dr Juan M. Allende, professor of clinical surgery in the University of Cordoba, Argentina, he told me that the surgery of trauma in South America is carried on exclusively by specialists, and the specialty is known as the surgery of traumatologia and orthopedia.

My effort tonight will be to call your attention to these changing conditions in the surgery of trauma in this changing world, and try to interpret them from the viewpoint of the general surgeon.

Interest in major trauma is being constantly stimulated in these days by military, industrial, and automobile catastrophes. During a similar crisis, under the pressure of the first World War, improved methods of fracture and wound treatment were instituted. Some of these methods, in the original or modified form, were promptly incorporated into the accepted lore of surgical treatment, while others have been discarded long since, for example, at the present time the elimination of Dakin's

solution from the United States Pharmacopeia is being discussed seriously.

¹ We are now faced with the probability of having to care for large numbers of war casualties, and it is apparent that in this war the surgical problems will be more complex than in the previous wars. The absence of armadas and panzer units, which attack the civilian population over large areas of a country, spreads the casualties to the non-combatant population. In the present European struggle it is reported that civilian casualties have been ten times more numerous than have military, as a result of the bombing and shelling of cities. There are new types of injuries, and the wounds caused by the modern high explosive shells and bombs, whose fragments have terrific velocity, tend to be massive and more devastating than the wounds of former wars. The blast injuries resulting from bombs of this type require attention which was not even suspected in the last war (Fig. 1). They result from a high pressure wave, which is immediately followed by a low pressure one, and the injuries usually take the form of capillary hemorrhages of the lungs (Figs. 2 and 3), the liver, the spleen, intestines, adrenals, and kidneys.

² A second reason for particular interest in the problems of fractures and trauma at this time is the increasing pressure being exerted by the economic front of the workmen's compensation legislation. Methods of treatment which will insure the ultimate restoration of function in the minimum length of time are now demanded by the compensation boards and insurance companies. This has led to higher standards of reduction, fixation, and after-treatment of fractures. This trend is also directly responsible for more widespread employment of open reduction and internal fixation. Though internal fixation was strongly advocated many years ago by Arbuthnot Lane, the difficulties of the technique and the meticulous equipment in personnel and material incident to the proper attainment of this type of fixation discouraged its general use. Only recently have we realized the vital importance of the rigidity provided by internal fixation, which makes possible active motion



Fig. Wounds of the face resulting from high explosive bombs. (Courtesy of M. Broster)

of the affected extremity immediately after the operation. This ideal can now be obtained through the employment of the biplane fixation which was devised by Clay Rav Murray of New York.

As internal fixation became more generally practiced it was quite evident that improvement was necessary in the type of metals used. The plates and screws became eroded and would lie loosely on the bone fragments. It was Venable and Stuck who demonstrated that this erosion was due to the electrolytic action of tissue fluids upon the metals. They claim that when any two dissimilar metals are used as fixatives in the same wound an electrolytic process is set up between these metals in accordance with the laws of electromotive force. Vitallium was proposed by them as a metal entirely inert to the effects of body fluids when not associated with any other metallic substance. As a result of this research vanadium has been discarded as the standard metal for plates and screws and in its place vitallium or high-chrome low nickel steel, or tantalum are now in vogue.

3. Motor accidents provide the third need for increased interest in fractures and traumatic wounds. More stringent traffic regulations of all kinds are needed to stop this terrible waste. It is without question the responsibility of the medical profession and surgeons in particular to see that this evil is corrected. Legislation, publicity and the direct fostering of organizations such as the Red Cross, together with the guidance of state highway commissions in instructing laymen in the proper methods of administering intelligent first aid care to the victims of industrial and automobile accidents, are necessary to promote the interest of the laity in the subject.

A sign encountered this summer while motoring through New England indicates the responsibilities which motor accidents are bringing to the rural physician and surgeon, and the economic burden being thrust upon communities, many of which are unequipped and financially unable to bear them. A large billboard was found at the entrance to the town, which read "This town does not maintain a hospital, and motorists are warned that they should take every precaution to avoid accidents while driving through, for we are not equipped to take care of them. This may be the easiest way out, but I am sure it will not be the final answer even in that town. Nor should it be."

During September 1941 3,777 persons met death as a result of motor accidents in this country. This was an increase of 14 per cent over the same period last year and marks the fourteenth successive month to show an increase over 1939 and 1940. With 1941 three-quarters gone the total killings have been 27,860 which is a rise of 17 per cent over the fatality list for the same period of 9 months in 1940.

After this brief consideration of some of the many special fields of knowledge which must be mastered in order to cope with the changing problems in the treatment of traumatic wounds and fractures one might think that we had forgotten our original promise. On the contrary, it is exactly because of the complexity of these problems that we believe that a general surgeon employing the basic knowledge of the principles of surgery should be better

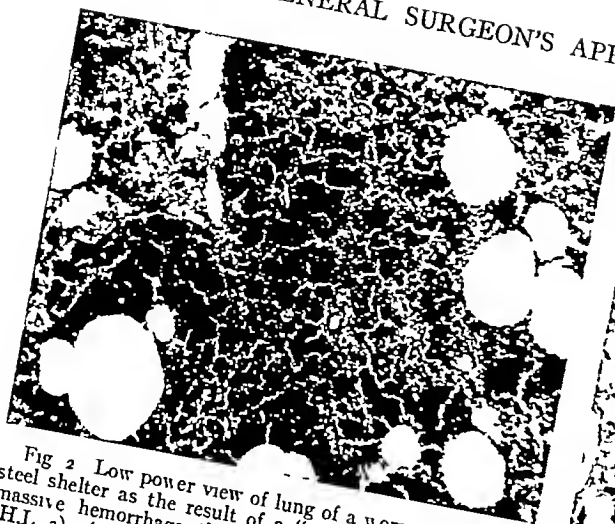


Fig 2 Low power view of lung of a woman killed in a steel shelter as the result of a "near miss" There was massive hemorrhage throughout the left lung $\times 58$ (H.L. 3) (Courtesy of Mr Broster)

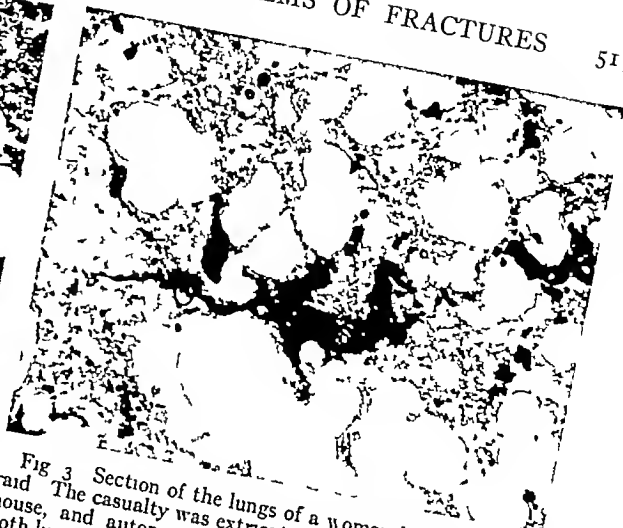


Fig 3 Section of the lungs of a woman killed in an air raid The casualty was extricated from the remains of her house, and autopsy revealed numerous hemorrhages in both lungs The specimen has been stained with scharlach R (black regions) to demonstrate fat $\times 58$ (H.L. 5) (Courtesy of Mr Broster)

fitted to arrive at a complete solution of them than are his more highly specialized colleagues

FIRST AID

I feel sure no one will disagree with the statement that the first essential in treating a patient suffering from a fracture or trauma is to try to evaluate the condition of the patient as a whole, and not to concentrate entirely on the local wound or deformity, immediate or final Age, sex, physical development, nutrition, emotional status, all of these elements and many more must be grasped at the same time as one prepares to administer proper first aid care I say proper first aid care because —while the beneficial effects of such aid as immediate splinting of fractures or dressing of wounds is unquestioned—the methods of carrying out this first aid may be far from ideal

May I offer here the slogan which we advocated and taught to the lay public during the last war, and to Red Cross groups during the interval between the two wars namely, when in doubt as to what you are dealing with, do nothing, and when you are not sure about what should be done, even though you know the indications, do nothing Those of us who do not see these patients until after the administration of well intentioned first aiders know too well that the patient too often would have been in better condition if he had

been left alone and had not received the treatment given to so many of them Dr William Darrach has expressed this in a more scholarly way "In our early examination and treatment we should be guided and restrained by our realization of the pathology, by the mental picture of what has actually occurred beneath the skin, and what may occur as a result of our first aid efforts "

Gentleness is unquestionably the keynote of first aid care and must be rated above all other considerations in the management of severe accident cases

Hemostasis In dealing with traumatic wounds it is frequently necessary to control hemorrhage This is accomplished most easily and with the greatest safety by applying a pressure dressing The latter should be firm, but not excessively so Tourniquets are sometimes required to control more severe hemorrhage, but only as a last resort, and one must not forget that periods of release are required if the band remains in place for more than 30 minutes Gangrene is still too often the result of the application of tourniquets by conscientious first aiders

Asepsis is secondary only to the control of hemorrhage in the primary treatment of open wounds As a first aid measure the application of a sterile or mechanically clean dressing is the best safeguard against infection Anti-



Fig. 1. Wounds of the face resulting from high explosive bombs. (Courtesy of Mr. Brower.)

of the affected extremity immediately after the operation. This ideal can now be obtained through the employment of the biplane fixation which was devised by Clay Rav Murray of New York.

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more time must be allowed by the schools for the teaching of traumatic surgery, and fresh material of this sort should be made available to the students. As far as we know, Dr Galle of the University of Toronto was among the first to recognize this need and to make an effort to meet it.

The important elements of this subject cannot be learned in lectures and in dry clinics by viewing the bandaged wounds and splinted extremities. Students must see, and participate, if possible, in the whole procedure from the time the patient enters the hospital until his wound or fracture has been treated and he has been put to bed on the ward. In hospitals, internes and residents require special instruction in this field, and this can be made possible by spending a specified time on a traumatic service. The special value of a traumatic service has been proved to our satisfaction, and in such a plan the traumatic cases are segregated into special wards and cared for by a group of nurses and attendants specially trained in handling the equipment and problems incident to fractures and major injuries.

Probably this ideal cannot be achieved generally because of the financial outlay which it entails. However, it is usually possible, at least, to practice a modified version of the idea by having traumatic cases under the care of the same surgeon or group of surgeons continuously for a period of 6 months, or preferably a year. In this way the plan of treatment undertaken is not as likely to be interrupted as when the direction of the service is changed at shorter intervals. Upon discharge from the hospital it is also advantageous to have the same team to carry on in the out-patient department. Both fractures and major traumatic wounds are treated intelligently only if they are followed carefully for prolonged periods after discharge from the hospital. The results of epiphyseal injuries, shortening or tilting of long bones, restoration of joint function, and contraction of scars, to mention only a few instances, cannot be evaluated fully until at least one year after the actual treatment has ceased. Such an organization may seem cumbersome and unwarranted to those who have not seen it in action. This may be true for a short time after its in-

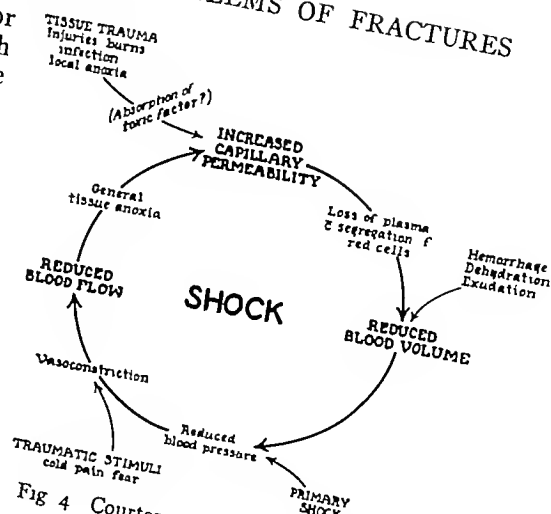


Fig 4 Courtesy of Dr Norman E. Freeman

ception, but once established the results are so greatly improved that the satisfaction to both the patient and the surgeon is a sufficient stimulus and compensation to keep it running smoothly.

Undoubtedly one of the most perfect demonstrations, not only of the possibilities but also of the efficiency that can be obtained by the specialization of the surgery of trauma and fractures, is to be seen in the fracture service of Darrach and Murray at the Medical Center of Columbia University in New York. In referring to such an ambitious plan for the teaching of undergraduate, graduate, and postgraduate surgery of this type, one must pay homage to this contribution to the problems of traumatology.

Time will not permit of an exhaustive discussion of the many interesting phases of this subject. However, we have chosen three, namely, shock, burns, and compound fractures, for more detailed consideration.

SHOCK

In the discussion of shock the general surgeon must always define his understanding of the pathology of the process in order to justify the type of treatment used (Table I, Fig 4). We subscribe to the now generally accepted theory that shock is caused by one, or several, or all of a group of factors operative at the time of the injury. These factors are hemorrhage, dehydration, pain, cold, fear, asphy-

TABLE 1 — SHOCK

Cause	Treatment
Hemorrhage	Transfusion
Dehydration	Fluids
Pain	Morphine
Cold	Warmth
Fear	Reassurance
Asphyxia	Oxygen
Exhaustion	Rest

(Courtesy of Dr. Norman K. Freeman.)

septics probably do more harm than good when introduced into a potentially infected wound. Cleansing of the skin area around the wound should be left for the operating room inasmuch as proper solutions and the facilities for using them will probably not be available at the locus of the injury.

Simple methods There is a tendency among general surgeons who treat many traumatic wounds to utilize relatively simple and conservative methods. Soap and water cleansing of the skin surrounding a wound and irrigation of the wound proper with normal saline solution or sterile water should be used more often than complicated antiseptic skin preparations and antiseptic irrigants. Wounds of soft parts of the extremities should be splinted, not only to prevent pain and hemorrhage but also to discourage the spread of contaminating bacteria.

What appears now to be an epochal contribution in the control of infection in traumatic wounds is the experimental work of Trueta, which was undertaken with the object of explaining the localization of wound infection when the traumatized tissues were primarily immobilized in plaster. In two series of dogs, one being used for control and the other for experiment, the extremities in both groups were traumatized, the soft tissues lacerated and the bones fractured. The injured tissues were then inoculated with the *Bacillus welchii* perfringens and hemolytic streptococci. Following this the wounds were filled with sulfanilamide powder and packed open with vaseline gauze. In the control group the traumatized extremities were not immobilized while in the other group they were encased in plaster casts.

In the control group every animal died from a gas bacillus infection within 3 days while in the other group no deaths occurred. Tru-

eta explained this by the fact that the immobilization of the soft tissues resulted in stagnation of the lymphatic circulation. In the tissues of the animals examined after death he found, in the group with freely moving extremities the previously injected bacteria or their offspring had entered the blood stream within 24 hours after receipt of the injury. In the group in which the tissues had been immobilized the organisms remained within a short distance of the traumatized tissues but had not entered the lumen of the blood vessels.

FRACTURES

In the treatment of fractures the simplest technique which will afford adequate reduction and complete immobilization should be chosen. Open reduction with internal fixation is recognized as an ideal procedure for the treatment of simple fractures, but should be reserved for exceptional cases. Furthermore unless one has occasion to practice open reduction with internal fixation frequently we believe it is better not to attempt this procedure. It is usually not performed successfully by the occasional operator.

In summary we will repeat that our endeavor in treating traumatic wounds is to avoid intricate or cumbersome techniques and to adhere carefully to the fundamental principles of gentleness, hemostasis, asepsis, and immobilization.

It may be well to insert at this point a word about one phase of the treatment of fractures and traumatic wounds which has troubled the surgeons who form the Fracture Committee of the American College of Surgeons, namely the need for an educational program aimed at improvement in the care of trauma of all kinds.

Such a program must have its origin in the medical schools where more emphasis should be placed upon the recognition and management of various types of fractures and traumatic wounds. Furthermore medical students should be taught to recognize the types of cases which they will not be qualified to handle as general practitioners and which should be referred to one specially trained in surgery. In order to accomplish these aims

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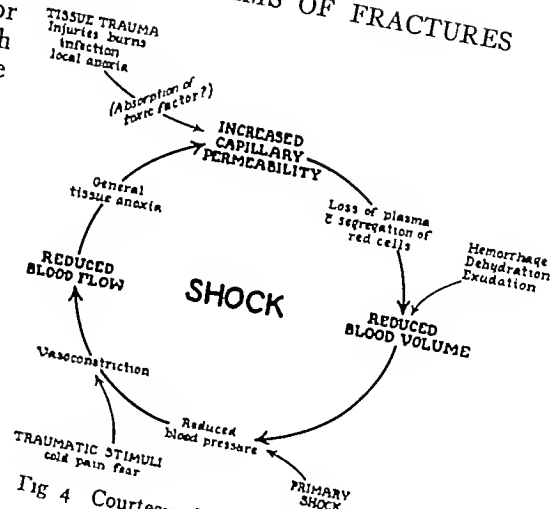


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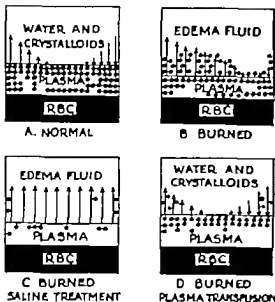


Fig. 5. Distribution of fluid between the capillary and tissue spaces.

is, and exhaustion as outlined by Freeman. The total effect of this phenomenon is to produce tissue anoxia which gives rise to abnormal capillary permeability. Consequently there follows a loss of blood plasma, a diminished blood volume, lowered blood flow, blood stasis in the capillaries, and finally a greater

degree of anoxia of the tissues. In this manner a vicious circle is established which can be broken only when the proper treatment is administered.

Treatment of this condition up to very recent times consisted of relieving the objective symptoms by means of well known methods.

About 10 years ago the intravenous infusion of saline and glucose was added to the armamentarium. This resulted in a temporary rise in the blood volume and blood pressure which was not sustained because the fluid left the leaking capillaries almost as fast as it was introduced and carried with it the vital serum protein so that the harm which was done was not only passive but was likewise active (Fig. 5).

Following this routine use of saline and glucose, whole blood was infused into veins in order to raise and maintain for a length of time the flagging blood pressure. It is true there are definite indications for the use of whole blood in shock, particularly when it is associated with hemorrhage but the difficulty in performing transfusion into the collapsed veins of the shocked state have been experienced by every surgeon. In this connection we wish to call attention to the recent work of Tocantins in Philadelphia. During

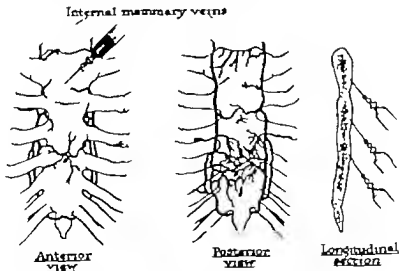


Fig. 6. Illustration of the distribution of the dye in the retrosternal veins, and the location of the needle during the injection. (Courtesy of Dr. L. M. Tocantins)

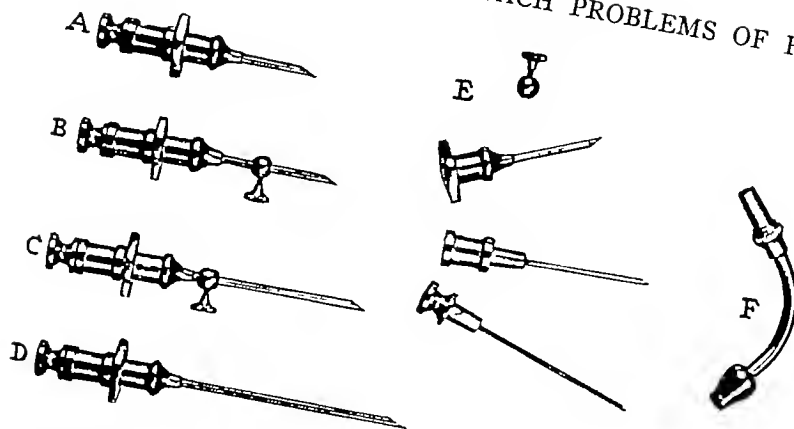


Fig 7 A, B, C, D, infusion needles of various lengths E, component parts of a needle, from top to bottom needle guard, external needle gage 15, internal needle gage 18, solid stylet F, curved adapter (Needles made by the George Pilling Co, Phila delphia)

the stage when fluids are most urgently needed, the physician is left without ready access to the central portion of the circulation because of the collapse of the peripheral veins as a result of shock. It occurred to Tocantins that under such conditions the bone marrow offered the ideal site for the introduction of fluids until the patient reaches such a stage that the peripheral circulation is restored and access to the veins is again possible. Since the marrow veins are surrounded by a rigid envelope, they are less likely to collapse, and probably can withstand forcible injection, without overdilatation and leakage, better than the poorly supported peripheral veins. Further, substances injected into the bone marrow cavity are taken up almost immediately into the venous circulation and apparently unchanged (Fig 6).

"We have experimentally demonstrated this by the injection of dye into the marrow of the sternum of a cadaver and found that it rapidly appeared in the right auricle. The comparatively short distance between the sternal marrow and the right side of the heart makes this possible. The rapid introduction of fluid into this side of the heart may, therefore, help to restore the cardiac output during the phase of acute peripheral failure, by increasing the

volume of the blood returning to the central portion of the circulation."

Tocantins needle (Fig 7) After the needle has been inserted through the cortex and the marrow has been obtained by aspiration, the syringe containing the material to be administered is connected with the needle and the material is injected as fast as the resistance offered to it will allow. In conscious patients, if the fluid is injected at a rate greater than 10 cubic centimeters a minute, there is usually a feeling of fullness in the sternum which, however, passes off immediately upon cessation of the injection. By using a two-way valve, one side connected by rubber tubing to the container of the fluid and the other leading from the valve into the sternal needle, it becomes unnecessary to remove the syringe from the sternal needle every time it has to be filled. In some instances, in which a more rapid rate of injection is desirable, two needles can be introduced into the sternum, one at either end, and since the marrow cavity of the manubrium and the marrow cavity of the sternum seldom communicate, it is possible to inject material through one orifice without it coming out of the other. This method can be used for the administration of any type of medication to patients with acute circulatory fail-

PLASMA VOLUME

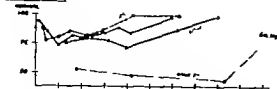


Fig. 8. Illustration of the shifting of the plasma volume in a series of burns with local treatment only.

ure and it has been found to be much more efficient than when the material is injected by other routes.

In the 73 cases in which this method was used by Tocantins no untoward reactions of any kind were experienced.

But there are definite contraindications to the use of whole blood transfusion to combat shock which are readily understandable if one accepts the etiology of shock as outlined here. Whole blood infusions will provide an increase in blood volume but they also supply an element which is detrimental in shock—the red cells which when added to the circulation serve to increase the viscosity of the blood and thus cause greater capillary stasis. This in turn brings about a greater degree of anoxia and increases the capillary permeability. To put it briefly, whole blood transfusions are contraindicated in shock because they tend to exaggerate the existing hemoconcentration. Hemoconcentration however may be absent and not marked when shock is associated as the result of hemorrhage.

The search for a substitute for whole blood, which would raise the blood pressure by increasing the blood volume without increasing hemoconcentration, was terminated happily when the use of blood plasma was suggested. As early as 1917 Strumia first advocated the use of blood serum in shock treatment, but adverse reactions, since found to be due to the absence of the fibrin fraction, caused serum to fall into disrepute. Then in 1929 he found that plasma was equally effective in combating shock and did not give rise to reactions. Ten years were to pass before the plasma transfusion was widely accepted and employed in shock treatment, but now this therapy is well established. It has stood the test of the demands of war surgery and answers the physiological requirements of the damaged

PLASMA VOLUME

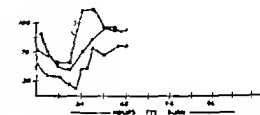
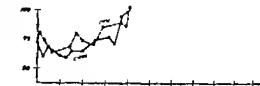
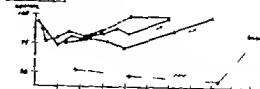


Fig. 9. Comparison of the duration of the shifting of the plasma into the perivascular tissues. Above: When local treatment only is used. Middle, when local treatment and blood transfusions are used. Below: when local treatment, blood transfusions, and adrenal cortical extract are used.

tissue. Plasma dilutes the concentrated blood of the capillaries and tends to remain in the vascular bed better than any other material thus far used.

The history of the production of plasma for infusion in shock states is interesting but too lengthy for consideration here. The preparation of plasma from citrated blood is now accomplished both by centrifuging and by the simpler natural settling process. After preparation the plasma is probably best used in its liquid form, although dried and frozen types of plasma are available. One other interesting development has arisen from this plasma industry. Plasma, once an incidental dividend of the blood bank system, has now become the capital of that system. The demand which is made for plasma is now commonly stated as being four times that for whole blood.

When the use of plasma in the treatment of shock was generally established, it became necessary to discover some way of testing

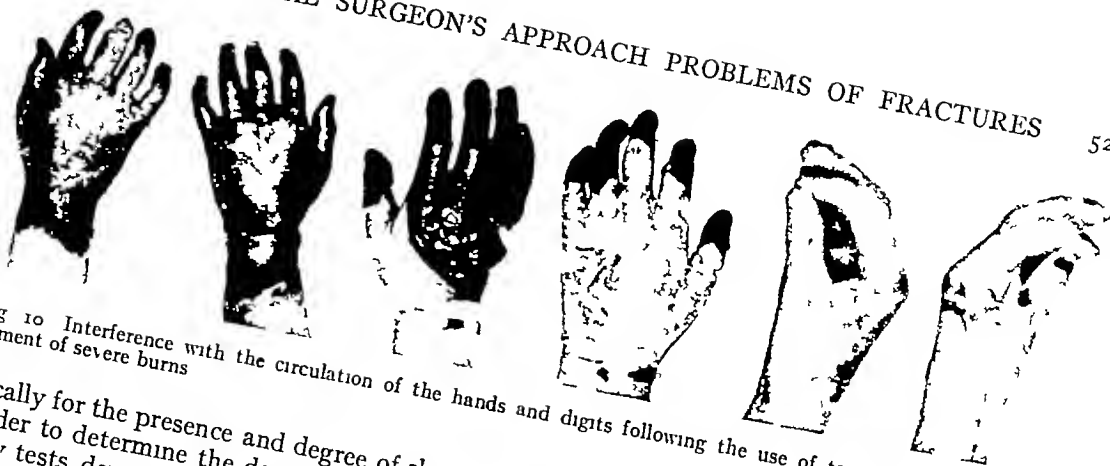


Fig 10 Interference with the circulation of the hands and digits following the use of tannic acid in the local treatment of severe burns

clinically for the presence and degree of shock in order to determine the dosage. The laboratory tests devised for this purpose consist of the usual hemoglobin and hematocrit determination and red blood cell counts. From a consideration of these figures the state of hemoconcentration may be determined.

More recently these values have assumed added importance in that with them one can compute by means of a simple formula the amount of plasma lost. Thus replacement of plasma is removed from the realms of uncertainty and carried out on a definite volume basis. An example of such a formula is that of Black which is given as follows

$$\frac{HB}{100} = \frac{5}{5X}$$

HB is the observed hemoglobin
X is the plasma lost in liters

This formula has been criticized from the point of view that it fails to take into account the fact that the hemoglobin may be very low in shock associated with hemorrhage in which there occurs a compensatory dilution of the blood. However, the formula has been of great value in emergencies and especially in war conditions when one cannot wait for or obtain more complicated tests. If the formula cannot be recalled it is a safe rule to give plasma to any patient in a shock state when the hemoglobin is found to be above 100 per cent.

When laboratory facilities are available for determining the hematocrit and plasma protein concentrations, we have found the following formula devised by Elkinton, Wolff,

and Lee to be more accurate than that of Black.

For calculating this quantity, the authors have proposed the following formula

$$\text{Plasma protein requirement in grams} = 3.5 W - \frac{W(100-Ho)HnPo}{2(100-Hn)Ho}$$

W = body weight in kilograms
Hn = normal hematocrit value, per cent cells
Ho = observed hematocrit
Po = observed plasma protein

If the plasma protein requirement in grams is multiplied by 14 the required volume in milliliters of plasma is obtained



Fig 11 Second and third degree severe burns of the forearms and hands, treated with tannic acid, on the right, and with triple dye, on the left

to apply successfully and, when applied as one of the various pedicle or flap grafts, the procedure is lengthy but the chances of success are improved. From a cosmetic standpoint the full thickness skin graft cannot be surpassed.

COMPOUND FRACTURES

Every compound fracture is potentially infected and therefore must be treated as though actually infected. This statement will not be questioned as regards grossly dirty wounds, but in cases of wounds with no external evidence of contamination there is disagreement from some quarters. Without being certain of the cleanliness and asepsis of the bared fragments it is too often assumed that the innocuous looking wound of the skin will heal satisfactorily and the lesion is treated as a simple fracture. The occasional wound of this type which becomes infected is responsible for the bad reputation of compound fractures. Tinker quoted by Kennedy stated the problem very aptly in 1909—"The most important consideration in the management of compound fractures is still the wound of the soft parts. If our wound is aseptic, tetanus and blood poisoning are impossible, bony union and a movable joint are favored, osteomyelitis will not develop and a useful, if not perfectly normal extremity will usually be saved.

As a diversion for a few minutes perhaps you will allow me to offer two illustrations which will help to date the period to which Tinker and Kennedy make reference in the previous statement.

I was asked by the late Dr. Astley P. C. Ashhurst, during the year of the bicentenary of the introduction of Listerism into surgical technique to determine if possible and to illustrate by means of graphs, the effect of asepsis and of antiseptics upon the surgical practice of the Pennsylvania Hospital in Philadelphia.

At the Pennsylvania Hospital we have continuous records of every patient from the time of its opening in 1751 to the present. This is not even possible in the Royal Infirmary at Glasgow where the work of Lister was first carried out. The records of his work in their wards have been destroyed.

With this type of record and fairly constant factors, before and after statistics obtained from such a source should be of peculiar value.

Figure 12 shows the influence of antiseptics and asepsis on the number of amputations performed at the Pennsylvania Hospital before and after the introduction of Listerism. Figure 13 shows the influence of these two surgical principles on the total number of operations in the hospital during these periods.

Could a better statistical experiment be provided to demonstrate that the prophylaxis of wound infection is the prime concern of the general surgeon in the treatment of compound fractures. The best method of prophylaxis is thorough débridement before contaminating organisms establish infection which means that débridement should be performed within 6 hours after the time of injury. In a few selected cases it may be possible to débride successfully as late as 10 hours after contamination occurs but every minute saved is added insurance against infection. We must impress upon our colleagues that minutes spent in the hospital preparing for operation are just as precious as those that were spent in transportation of the patient from the site of accident to the hospital. Therefore we should strive to organize the various hospital services so that the care of compound fractures will be given priority over that of all other operative cases.

The methods of débridement are well known but a few remarks to emphasize certain points of technique may not be amiss.

The use of antiseptics, regardless of their innocuousness should be confined to the skin surrounding the wound. Antiseptics should never be applied to the wound proper. Normal salt solution is the strongest solution which should be allowed to touch the exposed tissues.

Cultures of the wound both aerobic and anaerobic, should be taken routinely at the time of the débridement if laboratory facilities exist. In addition some surgeons advocate taking smears to be examined during the course of the débridement for the immediate detection of gas bacilli.

All compound wounds should be irrigated thoroughly with normal salt solution during

and after débridement After the final irrigation they should be dusted evenly with one of the sulfonamide powders Recently we have used sulfanilamide for this purpose and no ill effects in the local lesion have been noted although several patients have shown rather marked toxic effects of a systemic nature It is claimed that sulfadiazine can be administered in much larger doses than any others of the group without causing toxic manifestations It is excreted slowly and consequently we have unintentionally achieved higher concentrations in the blood than needed In one case in which the concentration reached 21 milligrams per cent there were slight toxic symptoms which ceased when the blood level fell to 10 milligrams per cent Whichever drug is used in the wound it should also be given by mouth as soon as the patient is able to take oral nourishment, in order to maintain the concentration in the blood at the optimum level

On the question of wound closure we stand firmly with the conservatives The soft tissue wounds of all compound fractures are packed wide open with vaseline gauze Primary sutures would doubtless succeed in many cases—However, because of the horrible results—osteomyelitis, amputation, or death—which may occur in wounds which become infected after primary closure, it is our opinion that it is not fair to expose the patient to a risk such as this

Accurate reduction and complete immobilization are important The time for reduction of compound fractures is at the time of the débridement Most reductions can be accomplished under direct visualization and instrumental manipulation of the fragments while the soft part wound is open There is thus no excuse for inaccurate reduction Fixation of compound fractures is possible by several methods

When a nonpadded plaster casing will hold the fragments adequately this is probably the best and safest type of fixation It introduces no foreign material into the field of operation or into the proximal or distal portions of the affected extremity Because no special equipment or techniques are required this type of fixation is the one best suited to the occasional operator

A more positive scheme for maintaining rigid fixation is the two pin transfixion method advocated by H Winnett Orr A pin or wire is driven through the proximal fragment and another through the distal fragment By means of traction and countertraction on an orthopedic table, or on one of the special distraction apparatuses, the length and rotation of the affected bone are restored Then while the pins or wires maintain the reduced position a plaster casing is applied which incorporates the pins or wires by means of which a more rigid fixation than can be attained with simple plaster casing is effected

Perhaps the ideal method for maintaining reduction in compound fractures as well as in simple fractures is by means of biplane internal fixation performed simultaneously with débridement This type of fixation must be in two planes to be effective Frequently, the plates or screws must be removed before healing of the fracture has occurred because of infection However, in many cases it is possible to succeed in avoiding infection as a result of the rigidity afforded by internal fixation, and the fragments will unite just as rapidly as do simple fractures which are treated in a similar manner

We cannot leave this subject without mentioning the excellent work of Tructa in the recent Spanish War in his treatment of compound fractures by the Orr method His monograph we recommend to every surgeon practicing in the field of traumatology The theme which he emphasizes is that for war wounds the needs are débridement and complete rest of the tissues immediately following operation and during transportation, and infrequent dressings The best way to afford such conditions is by means of a plaster casing He treated 1,072 cases of open fractures of limbs by the typical Orr method There were 6 deaths and 976 good results This is the most convincing evidence which has as yet been offered for the excellence of this type of treatment

CONCLUSION

In conclusion, we feel sure that most general surgeons will claim that they are fully able to provide such service as we have out-

lined and the majority will feel that they do give such service. But do they carry this service as far as the orthopedists in their routine care of fractures? I refer to the painstaking personal follow up not only in the hospital but for months and years after the patient leaves. Is the general surgeon's aim—once a patient always a patient? In other words does he feel the responsibility for complete or as nearly complete rehabilitation as can be

provided through the routine use of multiple operations, gymnastics, the swimming pool, physical therapy and above all, occupational therapy? Is he as interested in the surgery of trauma as in that of the abdomen? If not, I am sure that patients in the future will not choose him in preference to the surgeon or an orthopedist who is. The question is not whether he *can* give the best service to such patients, but as Dr. Meeker queried *will he?*

A CRITICAL SURVEY OF TEN YEARS' EXPERIENCE WITH FRACTURES OF THE NECK OF THE FEMUR

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DURING the decade extending from 1930 to 1940 the fact that patients with fractures of the femoral neck may be rehabilitated in surprisingly large numbers gained wide acceptance. The enthusiasm which greeted this novel idea resulted in a vast array of techniques with relatively few careful analyses of the results attending the use of these various means of treatment.

This study of 110 fractures of the neck of the femur treated at St. Luke's Hospital during this period is an attempt to subject our experience to critical analysis and to dwell on our vicissitudes as well as our achievements. *Ad astra per aspera*, the motto of the state of Kansas, might serve as a text.

The first 50 of these patients treated during the first half of the decade have been previously reported, but they will be mentioned for contrast and to allow us to correct certain misconceptions which inexperience led us to postulate (1). These original 50 patients were treated by manipulation and application of plaster of Paris spica bandage or traction in a few instances.

In 1935 our first internal fixation of a fracture of the neck of the femur was performed. We adopted the three phlange nail devised by Smith-Petersen (4) and have never found any fixative agent to equal it. The metal used was originally stainless steel, but since 1938 we have used vitallium.

Smith-Petersen's open operative reduction and fixation of these fractures was followed in 14 patients, but the results were so disappointing that it was abandoned. It is to be hoped that other surgeons will in time publish their experiences with open reduction and internal fixation of these fractures. During this period of experimentation, we had 8 undis-

placed fractures of the neck of the femur, and since we had previously satisfied ourselves that these invariably did well if they were protected we merely kept them in bed 4 to 5 weeks and then allowed them up with a Thomas caliper splint with pelvic band and crutches. These patients have results that are in every way perfect.

Following our extremely unsatisfactory experience with open reduction, we turned in June, 1938, to closed reduction and internal fixation and since that date 38 patients have been treated in this manner with results which are greatly improved from every standpoint.

REDUCTION OF THE FRACTURE

In reporting the first 50 patients treated without surgery and in the light of a very meager experience with open reduction, the following conclusion was reached: "The chances of getting bony union with a useful hip may be greatly enhanced by open reduction, derotation of the femoral head where rotation exists, and internal fixation." This expression of opinion, backed up with but little experience, is quoted to reaffirm what now seem the important factors, namely, *reduction* of the fracture and *internal fixation*. If the fracture is reduced, such rotation of the head fragment as existed has been overcome.

The reduction of these fractures is by no means as simple as it sounds. It would seem that open reduction should guarantee the end to end apposition of the fragments, but with the instability occasioned by the dissection of the ligaments of the joint almost 50 per cent of these fractures so treated displaced during the process of nailing.

With closed reduction (3) the situation was greatly improved at once. There were 38 patients treated with closed reduction and internal fixation, and of these, 26, or 68 per cent, were practically perfectly reduced, and 6, or 16 per cent, were reduced so that the bony

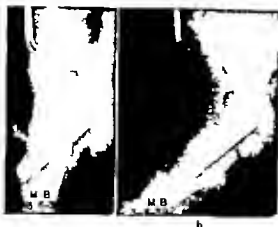


Fig. Closed reduction, end to-side nailing; union. 11th aseptic necrosis of femoral head. M. B. St. Luke's No. A 3700. Female 50 years old. Fracture of neck of right femur March 3, 1939. Reduced and nailed end to-side shown in 'a' and 'b'. End-rewelt 8 months after operation, marked aseptic necrosis of the femoral head, nail removed shown in 'c' and 'd'.



apposition was 75 per cent or better and 6 or 16 per cent, of these fractures were not reduced.

Of the 26 patients who had their fractures perfectly reduced, 22 survived and all of these had their fractures united, with excellent range of motion in the hip and few if any residual symptoms. Of those 6 patients who had 75 to 80 per cent apposition of the fractured surfaces, 5 survived and united, but 2 of these showed circulatory disturbance in the femoral head and all 5 had malunion with resulting deformity.

FAILURE TO REDUCE THE FRACTURE

It seems incredible but the fact remains that one half of the fractures treated by open reduction were not reduced when the nail was finally driven and the operation was completed. Since closed reduction has been prac-

ticed there have been 6 patients in 38 whose fractures have not been reduced. The reasons for these failures to secure reduction are worth recording in the 5 survivors.

1. A patient of 70 years of age whose reduction was attempted 10 weeks after injury and the fragments could not be mobilized. Non-union resulted.

2. A patient of 70 years of age whose fracture after repeated attempts, could not be reduced. Satisfactory roentgenograms were not obtained. Two weeks later a trochanteric osteotomy was performed and the patient has a useful hip.

3. Two patients had their fractures "reduced" with the aid of a fluoroscope and nailed. Check-up roentgenograms taken the next day revealed the situation that the fracture had not been reduced. This belongs in the department of locking the stable after the

CLEVELAND FRACTURES OF THE NECK OF THE FEMUR

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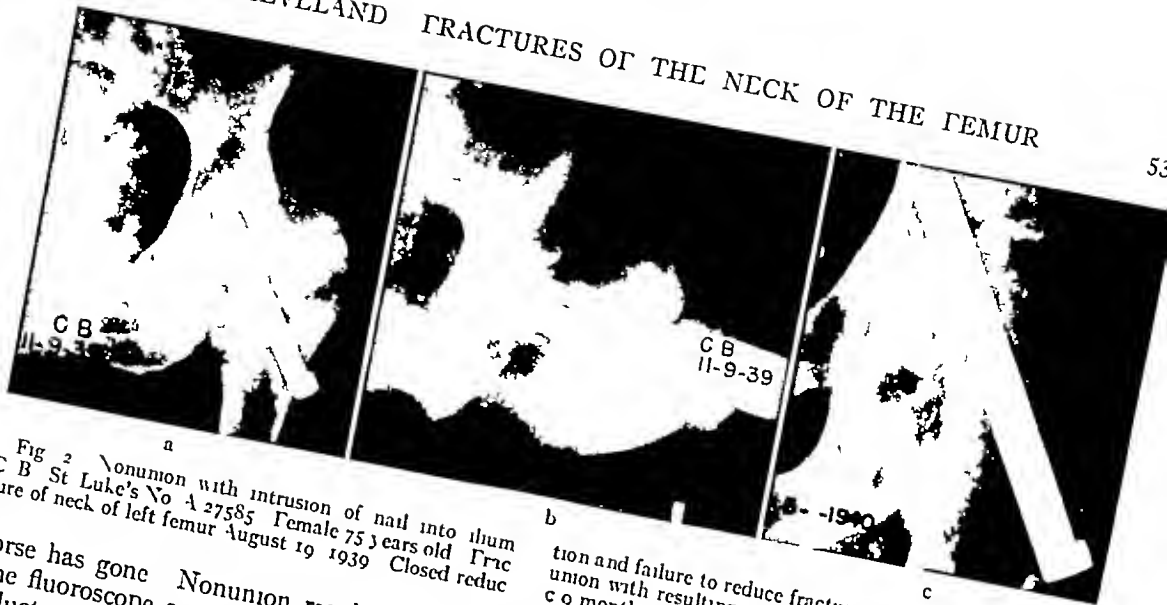


Fig 2 Nonunion with intrusion of nail into humerus
C B St Luke's No A 27585 Female 75 years old Frac-
ture of neck of left femur August 19 1939 Closed reduc-

tion and failure to reduce fracture shown in a and b Non-
union with resulting intrusion of nail into humerus shown in
c 9 months later

horse has gone Nonunion resulted in both
The fluoroscope serves no useful function in
reduction of these fractures, and its use is not
recommended

4 In one patient, a fracture thought to be
reduced with end-to-end apposition in two
planes, was nailed, and a more careful study
of the roentgenograms the following day
showed the fragments nailed end-to-side In
this patient the fracture united, strange as it
may seem, but then developed extensive aseptic
necrosis of the femoral head (Fig 1)

TECHNIQUE OF INTERNAL FIXATION

It is not the purpose of this presentation to
deal with technique, but it may be said that
the internal fixation of these fractures of the
neck of the femur may be readily accom-
plished without the aid of any gadgets what-
soever The proper insertion of the nail is not
altogether simple, and it is only with added
experience that confidence and familiarity
produce uniformly satisfactory results A nail
that is centered, or practically so, in the shaft,
neck, and head of the femur in both the an-

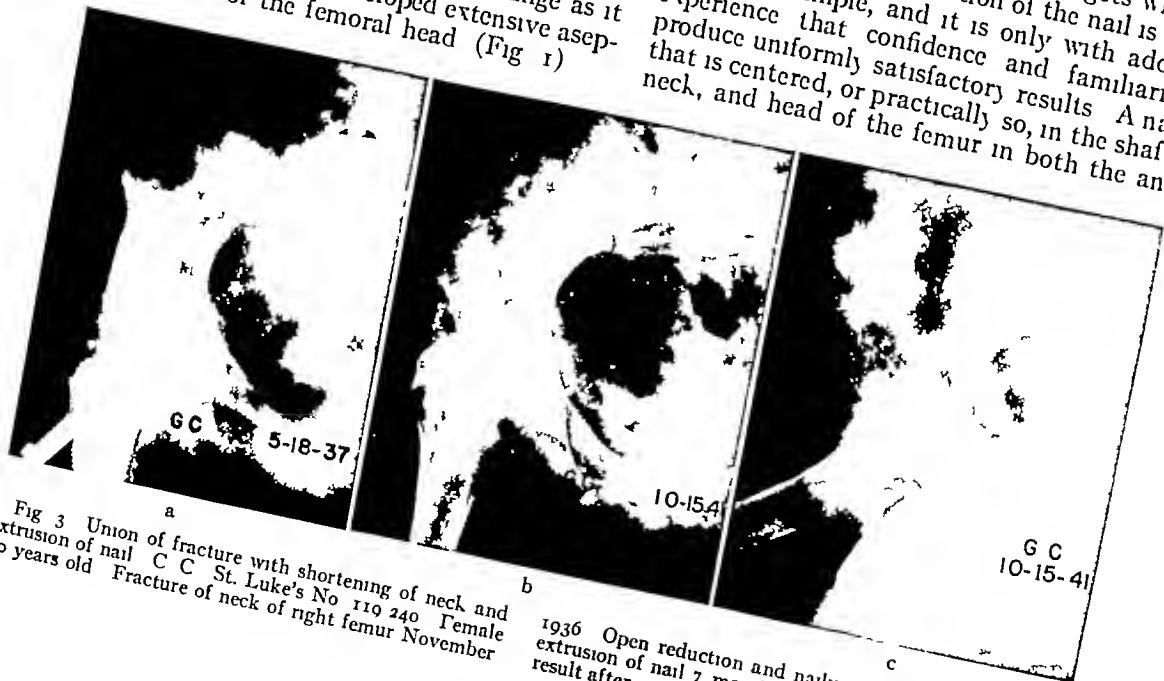


Fig 3 Union of fracture with shortening of neck and
extrusion of nail C C St. Luke's No 119 240 Female
80 years old Fracture of neck of right femur November

1936 Open reduction and nailing a, Shows union with
extrusion of nail 7 months after operation, b and c, end
result after 5 years, perfect except for slight shortening



Fig. 4. Nail overdriven at time of reduction and fixation. S. D. St. Luke. No. A 96434. Female 70 years old. Fracture of neck of right femur March 6, 1940. a and b, Show the closed reduction and the nail driven through the cartilage of the femoral head. c and d, Show the fracture united with the nail still protruding through the articular cartilage. This nail was removed. Result is excellent.

teroposterior and lateral planes, as shown by roentgenograms, is the optimum position. During the earlier years when open reduction was performed a centered nail was placed in only 5 of the 14 patients so treated, an incidence of 35 per cent. Later in the 38 patients treated with closed reduction an increased experience enabled us to center 21 or 55 per cent, of the nails driven. Among the entire 52 patients treated by internal fixation there were 16 instances in which the nail was centered and 26 instances in which it was off

center. Union occurred in 16 instances in which the nail was centered and in 18 instances in which the nail was off center. However the incidence of nonunion was almost twice as frequent when the nail was off center as it was when the nail was centered.

Three phlange nail. The length of this nail varies from 3 to 4 1/4 inches. The average patient requires a 3 1/4 inch nail and about half of our patients had a nail this long.

The metal of which the nail was made was stainless steel but in 1938 we changed to

CLEVELAND FRACTURES OF THE NECK OF THE FEMUR

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Fig 5 Open reduction, nailing excellent result almost 5 years later M S Female 68 years old Fracture of neck of right femur February 15, 1937 a, b, and c Show the fracture reduced, and nailing d and e, Show the end result 5 years later This is in all respects perfect

There has been no instance in which the nail broke
"Migration" of the nail There has been comment about the so called migration of the nail used for internal fixation This occurs chiefly in instances in which there is nonunion of the fracture In this series, there were 8 survivors with nonunion, and in none of these did the nail remain in its original position in the shaft, neck, and head of the femur Four of these nails extruded along the original path of insertion, 2 intruded across the joint line into the ilium, 1 simply disengaged from the head, remaining loosely in the shaft and neck, while the remaining one remained engaged in the shaft and neck, bridging across a gap to the head of the femur where it was reasonably firmly seated (Fig 2)
 When the fracture is solidly united, there is seldom seen any migration of the nail Among

the 34 united fractures which were nailed, there were 4 instances in which shortening of the neck as union progressed caused an extrusion of the nail along the path of insertion (Fig 3)
 There were also 4 instances in which the nail was originally overdriven through the cartilage of the femoral head This error is due to using a nail which is just about the same length as the shaft, neck and head pathway if driven flush and then blandly ignoring the fact that impaction of the fragments shortens the distance When a nail of such exact length is driven fully after impaction, it is bound to penetrate the articular cartilage There has been no further penetration of these nails (Fig 4)
Removal of the nail The nail has been removed only for cause Among those patients with united fractures, 2 extruded nails, 4 over-

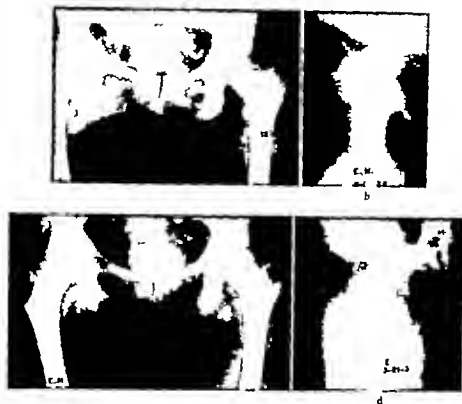


Fig. 6. An undisplaced fracture of the neck of the femur, nailed, excellent result. E. M. St. Luke's. A and B. Female 57 years old. C and D. Show fracture of neck of left femur without displacement. C and D. Show union of the fracture 9 months later.

driven nails and 5 nails in which the head of the femur showed evidence of circulatory disturbance have been withdrawn. In ununited fractures, the nail has been withdrawn in 4 of the 8 patients. In 3 of these 4 the removal preceded a trochanteric osteotomy.

Blaming the nail for failure to maintain reduction. It is our belief that instead of a certain tendency to blame the nail for failure to maintain reduction of the fracture the responsibility should be more properly charged to the surgeon's failure to obtain an original adequate reduction.

ROENTGENOGRAMS

The paramount importance of an exact and accurate roentgen ray technique cannot be overemphasized. The relationship of the shaft, neck, and head of the femur and the nail must be visualized during the reduction

and nailing by means of roentgenographic films taken in anteroposterior and lateral positions. With a portable roentgen ray apparatus and a developing room adjacent to the operating room the time of operation should be reduced to a minimum.

THE PATIENT WITH A FRACTURE OF THE HIP AS AN OPERATIVE RISK

There was but one operative death, an incidence slightly under 2 per cent. This was an elderly hypertensive diabetic woman who was kept in the hospital under treatment for a week prior to her operation. She died 4½ hours after operation of shock and cardiac failure.

Wound healing has, in all instances, been prompt, uncomplicated, and without infection.

These patients subjected to reduction and internal fixation have been kept in bed for 3

CLEVELAND FRACTURES OF THE NECK OF THE FEMUR

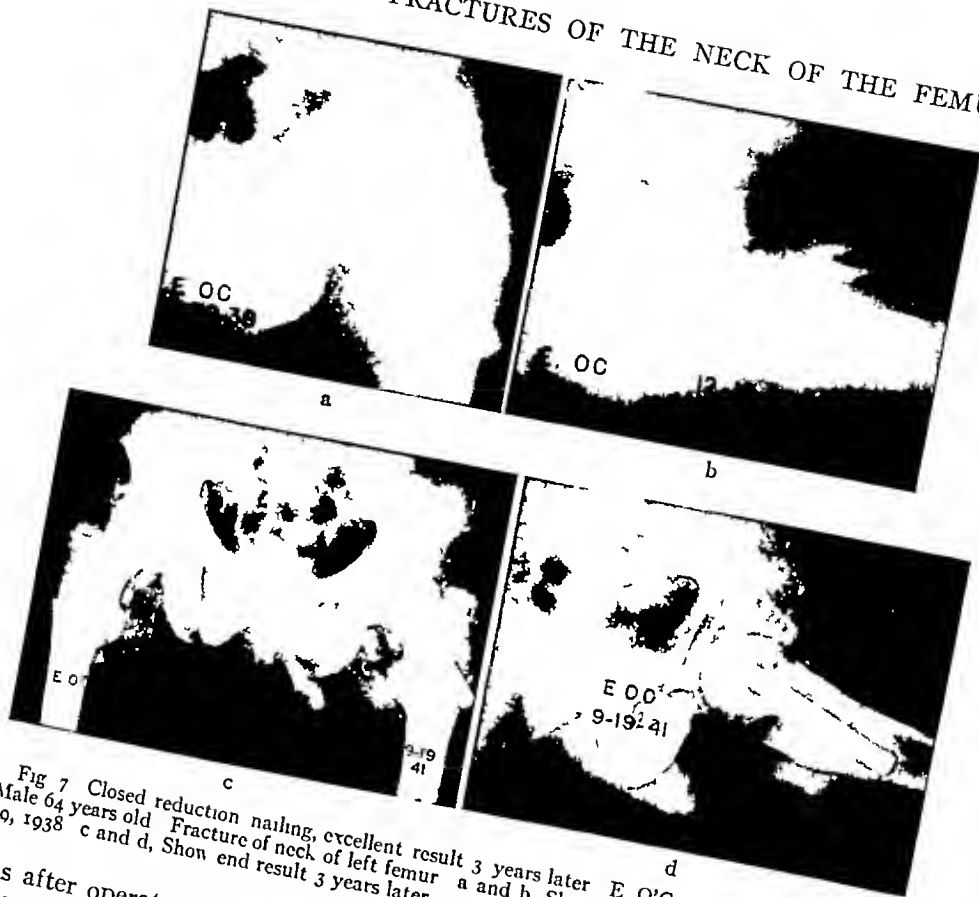


Fig 7 Closed reduction nailing, excellent result 3 years later E O C St Luke's No A 6937
Male 64 years old Fracture of neck of left femur a and b, Show reduction and nailing December
19, 1938 c and d, Show end result 3 years later

to 4 weeks after operation Russell traction just sufficient to balance the pull of the muscles, that is, 4 to 6 pounds total, has usually been employed, and they are without pain after 2 or 3 days. Getting these elderly people with broken hips out of bed on the first, second, or third postoperative day is a stunt and serves no useful purpose. When they are allowed out of bed, a Thomas caliper splint with a pelvic band is applied and crutches are used. These supports are employed until the fracture is united or definite failure to unite is established. Union of the fracture occurs from 4 to 9 months after reduction and fixation on the average.

The average hospital stay of the 60 patients treated since 1936 has been 46 days after operation. This should be compared to an average of 122 days for the ward patients and 135 days for the private patients in our first series of 50 patients on whom no surgery was per-

formed. The saving in time and expense to both hospital and patient is at once apparent.

FOLLOW-UP STUDY

This is an elderly group of patients, 80 per cent women, whose average age was 66½ years at the time they sustained their fracture of the femoral neck. Under ordinary circumstances there would be a considerable mortality in a similar group over a 5 year period. In the first group of 50 patients we had a 96 per cent follow-up, and in the present series of 60 patients we have a 100 per cent follow-up for an average of 23 months after the fracture for the 51 survivors. We know the end-result in every patient except one in whom sufficient time has not yet elapsed for solid union. Known 5 year results are not common, but we have 6 of them.

Mortality During the first 5 years there were 11 deaths.

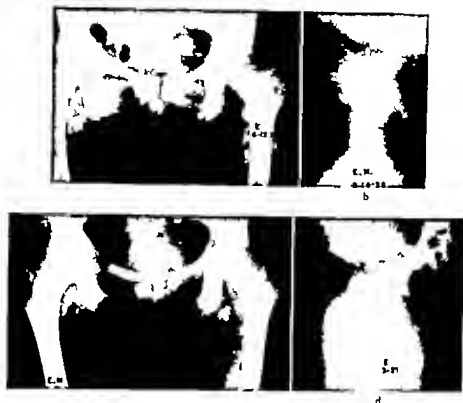


Fig. 6. A, Anteroposterior view of the neck of the femur united, excellent result. E. M. St. Luke's. N. A. 0010. Female 57 years old. and b, Show fracture of neck of left femur without displacement. and c, Show union of the fracture 9 months later.

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THE PATIENT WITH A FRACTURE OF THE HIP AS AN OPERATIVE RISK

There was but one operative death an incidence slightly under 2 per cent. This was an elderly hypertensive diabetic woman who was kept in the hospital under treatment for a week prior to her operation. She died 43 hours after operation of shock and cardiac failure.

Wound healing has, in all instances, been prompt uncomplicated and without infection.

These patients subjected to reduction and internal fixation have been kept in bed for 3

CLEVELAND FRACTURES OF THE NECK OF THE FEMUR

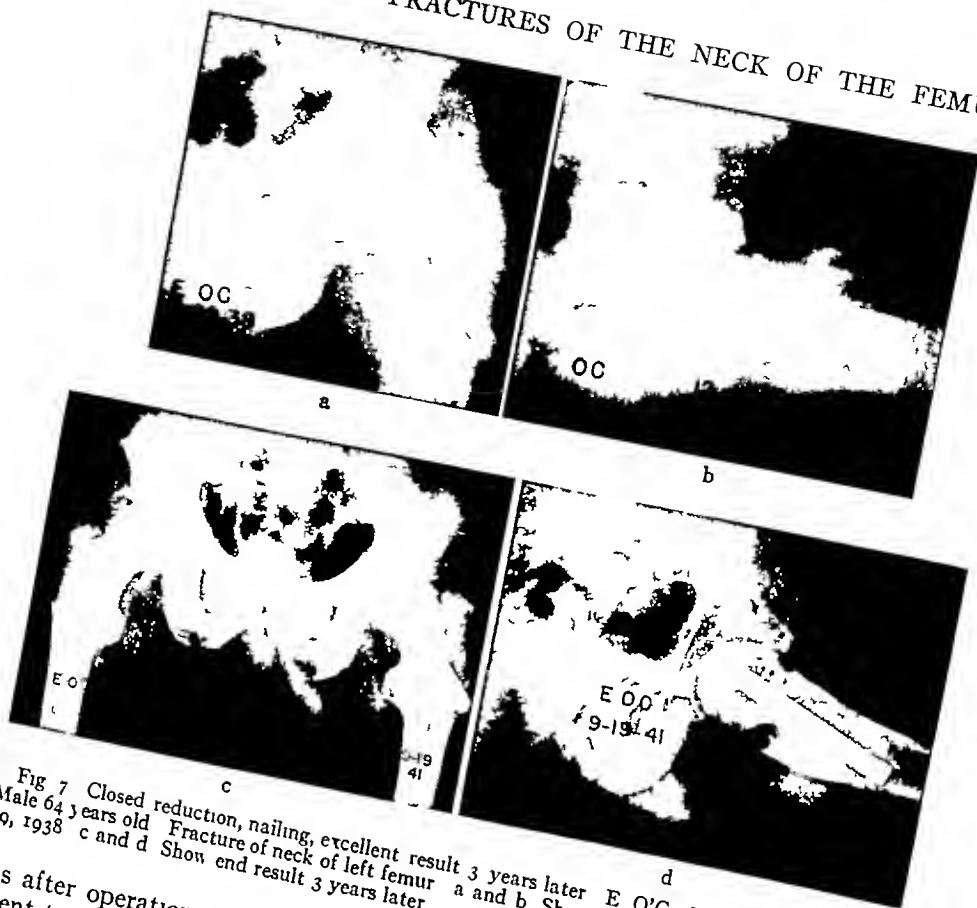


Fig 7 Closed reduction, nailing, excellent result 3 years later E O C St Luke's No A 6937
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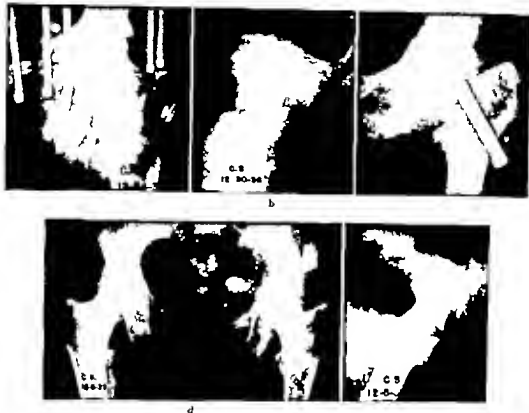


Fig. 8. Open reduction, nailfix, extensib. screw, ne. cross of femoral head. C. S. St. Luk. N. A. 02042. Female 50 years old. Fracture of neck of left femur open reduction. a, b and c, Show fracture, reduction, and nailfix.

ing December 24, 1936. d and e show the end result 3 years later after removal of nail. Some pain and limp. Patient has worn Thomas caliper brace for almost 5 years.

treated in the main by plaster-of-Paris spica bandage a gross mortality of 25 per cent. Four of these deaths were unrelated to the fracture which gave a mortality of 14 per cent attributable to the fracture. Among the second 60 patients there were 12 deaths a 20 per cent gross mortality with 3 deaths occurring 9 months to 3 years after the injury with the fracture solidly united in each instance. This leaves 9 deaths or 5 per cent, as the actual mortality due to the injury. It is interesting to note in comparing these 2 series of patients that operative surgery neither diminished nor increased the mortality in these patients with fractures of the neck of the femur. As might be expected, those patients who died were among the more advanced in years and 78 was their average age.

Union of the fracture. The known and widely accepted difficulty in securing union in these fractures until recently makes this subject one of absorbing interest. In the first series of 50 patients treated without surgery union with excellent function occurred almost entirely among those patients whose fractures showed no original displacement. Only 2 patients whose fractures were reduced by manipulation showed excellent anatomical functional, and cosmetic results.

The second series of 60 patients (52 treated surgically) whose results are herewith presented, shows a very different situation where the interpretation may be interpreted in all respects toward the better. These treated

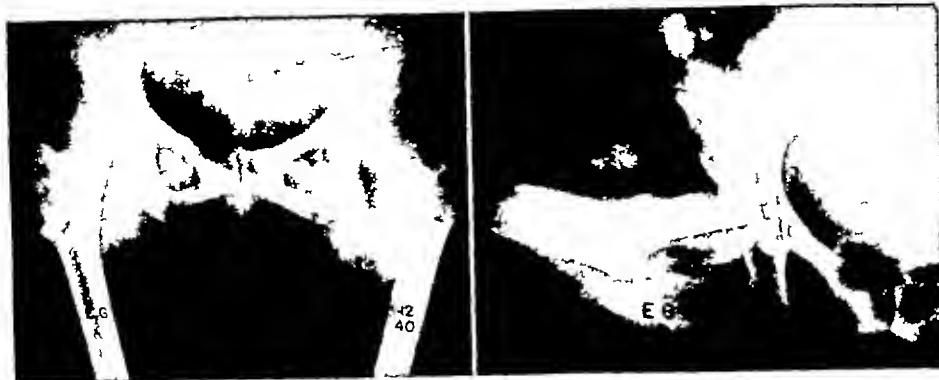


Fig 9a

Fig 9b



Fig 10a

Fig 10b

Fig 9 Closed reduction, union with mild condensing osteitis of femoral head E G St Luke's No A 5569 Female 53 years old Fracture of neck of right femur, closed reduction, and nailing October 15, 1938 a and b, Show the end result, union with slight condensing osteitis of femoral head 18 months later Patient is without symptoms An excellent result 3 years after operation

Fig 10 Nonunion of fracture treated by trochanteric osteotomy M D St Luke's No A36710 Female 70 years old Fracture of neck of right femur unreduced a, Shows the unreduced fracture, extrusion of nail b, Shows trochanteric osteotomy united, head of femur still ununited to neck A useful weight-bearing mechanism

only 2 of these, or 28 per cent, of those united were excellent results (Fig 5) The 8 undisplaced fractures treated without surgery were all excellent results from every standpoint (Fig 6) Among those patients treated by closed reduction and nailing there were 27 whose fractures united and 24 of these, or 88 per cent, of those united were excellent in every respect (Fig 7) while the 3 others had deformity due to malunion or varying degrees of circulatory disturbance in the femoral head sufficient to cause some symptoms

A comparison of the incidence of union in the two series of cases and of the various methods of treatment in the second series is shown in Table I

To make a long story very short indeed, union of fracture of the neck of the femur, in our hands, increased from 47 per cent of the survivors in the first half decade to 83 per cent of the survivors in the second half decade The credit for this must be ascribed to internal fixation and increasingly improved reduction of these fractures

Circulatory disturbance in the femoral head The recently completed study by the Fracture Committee of the American Academy of Orthopaedic Surgeons (2) speaks of the incidence and degree of arthritic changes in the femoral head encountered in these fractures The term arthritic changes is misleading, and I believe circulatory disturbance or change is

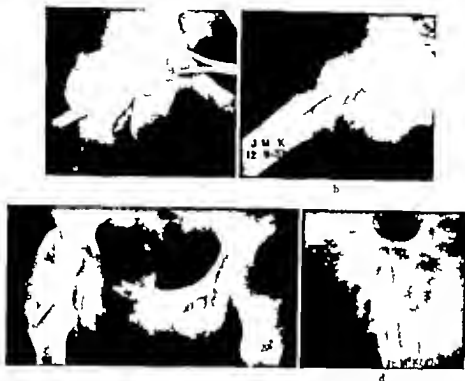


Fig. 8. Open reduction, malunion. (a) fracture bony overgrowth from the acetabular margin. J. McK. St. Luke's No. 4 3502. Female 67 years old. Fracture of neck of right femur December 7, 1937. (b) and (c) Show fracture and incomplete reduction. (d) Show malunion with bony overgrowth from the margin of acetabulum. 8 months after operation. This patient had a good and symptomless hip when last seen—years after operation.

preferable because arthritis of the hip is known and recognized in its various forms, while the alteration of the femoral head due to interference with its blood circulation is a different picture.

Actual arthritic change involving the hip joint following a fracture of the neck of the femur was found only once in this series of 60 patients.

These circulatory disturbances or changes in the femoral head may vary from a mild condensing osteitis to an advanced aseptic necrosis. In our experience they have invariably appeared within the first year after the fracture. We have had no instance in which the circulation failed after the first year had passed and union of the fracture was established.

The greatest predisposing cause of circulatory disturbance in the femoral head is non-

union of the fracture. Six of the 8 patients with nonunion showed extensive aseptic necrosis of the femoral head.

Of the 7 patients subjected to open reduction of their fractures which united, 3 had extensive aseptic necrosis of the femoral head an incidence of 42.8 per cent (Fig. 8).

Among the 27 patients with union of their fractures treated by closed reduction and internal fixation 4 had a very slight condensing osteitis (Fig. 9) and 1 had an advanced aseptic necrosis. Three of these 5 patients had incompletely reduced fractures. Of the 8 patients with undisplaced fractures treated without surgery none showed the slightest evidence of circulatory disturbance but 1 patient with an undisplaced fracture which was nailed showed definite circulatory disturbance.

One is forced to the conclusion in this series of patients, that the most important

TABLE I —INCIDENCE OF UNION AND NONUNION

Series 1 1910-1935 Nonoperative	Total in group	Union		Nonunion	
		No	Per cent	No	Per cent
Known	48	10	30	0	61
Living	38	18	47.4	20	52.6
Dead	10	1	10	0	0
Series 1916-1931 5 patients operated upon and 8 undisplaced fractures not operated upon					
A Open reduction and internal fixation					
Known	14	-	50	7	50
Living	10	6	60	4	40
Dead	4	1	25	3	75
B Undisplaced fracture—nonoperative					
Known	9	9	100	0	0
Living	8	8	100	0	0
Dead	0	0	0	0	0
C Closed reduction and internal fixation					
Known	17		73	10	27
Living	20	25	86	4	14
Dead	8	2	25	6	75
D Entire second series					
Known	59	42	71	17	9
Living	47	39	83	8	17
Dead	12	3	25	9	75

cause of circulatory disturbance in the femoral head has been failure to reduce the fracture and keep it reduced. For the benefit of those who feel that circulatory disturbance is more

TABLE II —INCIDENCE OF CIRCULATORY DISTURBANCE IN THE FEMORAL HEAD

	Total	Mild condensing osteitis of the femoral head		Aseptic necrosis of the femoral head	
		No	Per cent	No	Per cent
Patients with nonunion	8	0	0	6	75
Patients subjected to open reduction and nailing—United	7	0	0	3	42.8
Patients subjected to closed reduction and nailing—United	27	4	14.8	1	3.7
Patients with undisplaced fractures not operated upon	8	0	0	0	0
Total united fractures	42	4	9.5	4	9.5

frequent in the younger age groups, it may be stated that the average age of the 8 patients who showed this phenomenon together with union of the fracture was 62 years, $4\frac{1}{2}$ years under the group average. Those 6 patients with ununited fractures who showed marked

circulatory disturbance in the femoral head were 70 years of age on the average. The circulatory changes encountered among those patients may be summarized as follows, in order of frequency of occurrence:

NONUNION OF THE FRACTURE

This is a problem which is definitely diminishing but will doubtless continue to exist. The situation of these patients can be greatly alleviated as far as pain and instability are concerned by a trochanteric osteotomy of the femur. This operation has been performed on 3 of our 8 patients with ununited fractures with great improvement in their situation (Fig 10).

SUMMARY

Open reduction and internal fixation. In our hands, open reduction and internal fixation of these fractures of the neck of the femur offered very little improvement in end-results over those obtained by nonoperative means. Of the 7 patients whose fractures united, only 2 were wholly satisfactory. There were 3 cases of extensive aseptic necrosis and 2 bad mal-unions with marked deformity. In certain cases of open reduction, there occurred bizarre overgrowths from the acetabular margin, perhaps due to stripping of the periosteum (Fig 11).

Undisplaced fractures. During this period of tribulation in dealing with open reductions, the undisplaced fracture of the neck of the femur, treated by 3 to 4 weeks' rest in bed and weight-bearing after the application of a Thomas caliper brace, gave invariably optimum results. Since our nailing technique has improved, a number of these undisplaced fractures have been nailed without reduction.

Closed reduction and internal fixation. The accurate reduction by manipulation and the careful insertion of a three phlange nail has yielded surprisingly good results, union of the fracture in 86 per cent of the survivors. We make every effort to center the nail in two planes but are not always successful. Over-driving the nail through the articular cartilage of the femur has been done in 4 instances. It is due to carelessness and can readily be avoided.

Circulatory disturbance in the femoral head The circulatory disturbance in the femoral head, based on our experience with these 60 patients, has always appeared within the first year after the fracture. Seventy five per cent of the patients with nonunion of their fractures had extensive circulatory disturbance in the femoral head. Of those subjected to open reduction with their fractures united, 42.8 per cent showed extensive aseptic necrosis of the femoral head. Of those 27 patients with united fractures who were treated by closed reduction and nailing 18.5 per cent showed some evidence of circulatory disturbance, for the most part very mild. The majority of all patients showing circulatory disturbance in the femoral head with fractures united had inadequate reduction of the fracture.

Adequate reduction of the fracture We have found in this series of 60 patients that accurate reduction of the fracture is the most important single factor in securing union and avoiding circulatory disturbance in the femoral head. The actual or so called migration of the

nail is usually due to failure to properly reduce the fracture and this migration occurs almost exclusively in ununited fractures.

Nonunion Patients with nonunion of their fractures may be greatly benefited by a trochanteric osteotomy of the femur.

CONCLUSION

An accurate end-to-end reduction of a fractured neck of the femur by manipulation and fixed by a properly placed three-phlange nail should result in a very high percentage of unions, 86 per cent of the survivors in this series, and a low incidence of circulatory disturbance in the femoral head. This procedure is therefore recommended.

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FACTORS IN THE CHOICE OF MATERIAL FOR BONE PLATES AND SCREWS

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THE qualifications for determining and specifying the basic factors that are essential in internal fixation of fractures with metals should be defined. I see it there are three cardinal principles, three essential factors, which must be accepted and considered as a whole for the single purpose of securing and maintaining fixation without incurring changes that are detrimental to bone and that thus defeat the purpose of mechanical stability. These factors are (1) electrolysis (chemical), (2) physical properties, and (3) application.

ELECTROLYTIC (CHEMICAL) FACTOR

The entire change in our attitude and thought lies in the basic principle involved in the electrolytic factor. Without recognition of potential chemical changes resulting from the use of material affected by body fluids as the cause of deleterious effect upon bone, no matter how strong or how well applied the instrument used, a large percentage of delayed unions, nonunions, and marked bone necrosis as result of local decalcification and even osteomyelitis may be expected to occur.

I am aware that to delve at this time into all the whys and wherefores of electrolysis, the passing of electrons between metals of different potentials of electromotive force set in action by an electrolyte, and the series of changes that occur would not only bore you, but defeat the purpose of bringing about the broader understanding of the principle I desire to express, so I shall try not to be too technical.

Practically all of the so-called metals we use are a composite of different basic elements, each having a potential of different electromotive force and are known as alloys. They offer varying qualities of resistance to the given fluid to which they may be subjected, some

are more resistant to acids, others to alkalis, but in the variance of the degree of resistance electrons pass from one element to the other. Thus the atoms of one constituent are combined with or separated from those of the other through the mobilization of ions which is electrolytic action. When any alloy, generally referred to as a metal, is spoken of as being passive in a given fluid it is meant that that metal is so resistant to that electrolyte (fluid) that the passage of electrons is reduced to such a minimum that corrosion is practically nonexistent.

When plain iron nails were used in fractures (which is within my memory) they caused little trouble, but when metallurgists began to make steel out of iron by adding elements to it, our trouble began. After our first announcement of the result of a series of experiments in determination of the part electrolytic action had to play, an unfortunate statement was made in error on a similar occasion that "all the changes in bone resulting from the use of metals in fractures ascribed to electrolysis were simple oxidation and were not the cause of loosened screws, or the discoloration of tissue or excess of serous fluid, about the plates and screws," and unfortunately it apparently created a great deal of confusion.

When electrons are removed from an ion, atom, or molecule, the substance is oxidized; when electrons are added to a substance it is reduced. Thus every electrochemical change which takes place involves both oxidation and reduction.

If the difference is understood between one pure metal which is not subject to corrosion and a multiplicity of different metals combined into one (an alloy) which is subject to corrosion, then it is clear why a single screw or plate—unless it be of a single element—is no longer a single metal and why it will corrode unless made resistant to the fluid to which it is to be exposed.

Presented at the Symposium on Fractures and Other Traumas before the Clinical Congress of the American College of Surgeons, November 27, 1941.

I desire further to emphasize the point that different materials used in conjunction with each other such as the combination of passivated stainless steel screws in a vitallium plate etc. only serve to make stronger and more destructive batteries, though each may be inert if used separately. Only properly passivated steel should be used throughout or vitallium or tantalum should be used throughout. A combination of materials should never be used. An order to this effect has been issued to all Army hospitals by the Surgeon General of the Army.

It must be further understood that metals for use in surgery are passivated to be resistant only to blood serum or normal salt. For instance, 18-8 steel with molybdenum is resistant to solutions of sodium chloride but less resistant to bromine chloride and not at all to iodine chloride therefore the use of other chemicals in a wound, especially iodine in conjunction with metal fixation should be carefully avoided.

There are two recent articles in which use of Dakin's solution (hyperchlorite of soda) is advocated in the treatment of infected wounds in which compound fractures are plated to maintain fixation. Hyperchlorite of soda is a much stronger electrolyte than salt solution and may energize electrons not only in the substance of the plate but throughout the screws and so initiate destructive bone changes about the latter thereby causing an osteomyelitis otherwise avoidable.

Today there is increased interest and effort by metallurgists to create alloys that are as resistant to corrosion as possible for many industries as well as for bone surgery but the criterion of that resistance which we must understand and demand must be all the more carefully assayed for our use.

The manufacture of alloys is one of the most intricate of technical specialties. It is not so simple as having a formula, just placing the materials in an oven, and creating steel. More over because of the complexity of manufacture each batch turned out must be carefully tested to meet specifications and required standards.

We now have as a guide the basic principle that material must be sufficiently inert in the

body through its chemical resistance to the electrolytic effect of body fluids to remain inert. Through clinical experience and observation over sufficient time we have come to expect and to realize the necessity for the inclusion of this factor in any attempt to standardize the material to meet our requirements.

The Subcommittee on Education of the Committee on Fractures and Other Trauma of the American College of Surgeons, consisting of Drs. Huber, Wagner, Clay, Murray, and me is now actively engaged with metallurgists and the Bureau of Standards at Washington in the creation of such standards as are essential to meet our needs, based upon the practical absence of electrolytic changes and assured physical stability. The minimum requirements established are to be based upon results of tests of such materials as have been found to remain passive in experimental animals and in clinical cases for 2 or more years and upon tests of their physical fitness to withstand the stress and strain entailed. It is up to the metallurgists to create such material from available materials to meet these requirements.

PHYSICAL FACTOR

There is much more to the detail of the requirements of physical fitness than shape and size so that, though articles of different design may be added from time to time, all must conform to necessary specifications as to strength, ductility, malleability, fragility, torsion, and resistance to fatigue as well as resistance to corrosion which has been described.

The crucial failure of our previous effort to standardize plates and screws was to allow any manufacturer to produce them according to the formula sanctioned by the Bureau of Standards. The result was that vanadium steel plates appeared on the market with as many different characteristics and sold at as many different prices as women's hats.

The degree of heat applied in preparing the different metals to be combined, the difference in heat during the process, the manner and speed at which they are cooled, the way in which they are mixed as well as the selection of elements for use and the proportions, control the properties of the finished product.

Whether such metals are finished by machine or are cast, and whether or not the constituents are free from impurities, are factors which govern the price. Cheap, impure metal is the bargain stuff of the itinerant salesman. Is not success in attaining union of a fractured tibia worth more than the small difference in the cost of a plate?

The committee in its protocol of standards is not interested in low cost, or is it trying to meet prices. It is proceeding on the basic assumption that the surgeon desires only articles that will aid in the attainment of his goal and furthermore desires to be protected from unreliable gadgets.

The Pure Food and Drug Act protects us from impure chemical products. It is just as important, since we know what chemical and physical properties are essential for safety, that our patients and we be protected from metals that are unfit and may cause harm.

In addition to passivity, however, and to rigidity and strength it is most important that materials have varying properties, some must have machinability, others ductility and tensile strength so that the finest wires may be produced from them. In passing I will say that it is just as important for the abdominal surgeon to have passive material for wire sutures to bury in the tissue, though changes are not as obvious in abdominal surgery, as for the bone surgeon who uses the nail, even though the latter has the additional hazard of calcium changes due to electrolysis—splendidly termed by Masmontel "electrolytic osteitis."

APPLICATION

While chemical and physical properties of plates and screws can be made to conform to minimum standards their application in surgery cannot be controlled. Surgical judgment cannot be accurately measured nor technical skill standardized. Instead we can only point out principles for the application of plates and screws which will facilitate their use and will be most likely to ensure success.

Plates must be selected which are of sufficient strength and size to hold the involved bone. Small short narrow plates it goes without saying are inadequate for immobilizing a fractured tibia in a large adult. Before the

electrolytic factor was recognized in its effect in the decalcification of bone plates, such as the Sherman type, were made in order to minimize the volume of material, for it was recognized that the deleterious effect of metals seemed to be in proportion to the extent of metallic contact. Now we know that plates may be as wide or as heavy as necessary to meet the requirements of stable fixation. I think that the length of the plate should be at least three times the diameter of the bone involved to provide proper lever support. Moreover, the plate should be shifted about or bent until it conforms closely to the surface of the bone so that a tight grip may be obtained. Whether the plate is thick, or thin, wide or narrow, straight or curved, is unimportant so long as it fits snugly and is sufficiently strong to support the bone ends involved. It should be malleable enough to be bent and still tough enough to meet the strain required.

A single screw on either end of a plate beyond the fracture should never be used as it creates a hinge at the fracture site. Also a plate applied with two screws on one side of a fracture and only one screw on the other side is bad mechanics.

The drill holes for the screws should be about the same diameter as the shank of the screws. A drill slightly larger than the shank makes a hole in which the threads are insecurely anchored and likely to strip out of the bone. A drill slightly smaller makes a hole in which the screws cannot be inserted without great force. As a result, screw drivers slip, screws break, tempers are lost, and the whole operation may be ruined.

An exception to this rule is that a drill must be smaller than the shank of the screw when it is to be inserted in atrophic or decalcified bone. Obviously, in soft bone in which it is difficult to secure any sort of hold with a screw the chances of success are greater when the screws compress the cancellous bone into a more firmly compact media. Conversely the drill should be larger in very hard or curved bone.

The choice of the type of screw to use is easily made if several important points are borne in mind. In the first place long screws obtain a more secure mechanical grip on the

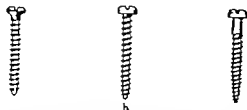


Fig. Types of screw. a, dowel; b, wood plain; c, pull up. Note the obliquity and wider thread of the wood type screw.

bone than short screws and engagement of both cortices of the bone is more likely to prevent motion of the fracture than if only one cortex is secured. Holes drilled entirely through the bone permit the ends of the screws to penetrate the opposite cortex and hold the plate firmly without impeding the tightening of the screws.

Whether one uses a Sherman type of screw with its dowel end that is supposed to drill its way or a machine type of screw rather than a more deeply threaded wood type is immaterial so long as a tight grip is obtained. I personally prefer the last as it seems to obtain better engagement and is easier to apply. Any of these types are applicable to plates in which the detail of counter sinking or special screw heads are subjects of choice.

There is, however, another type of screw (Fig. 1) which is important. This is the wood or "pull up" type of screw which has a smooth shank of the diameter of the thread between it and the head of sufficient length to reach through the proximal cortex. The reason for this is that when the threads have pierced the opposite cortex the distal fragment is drawn tightly against the proximal fragment as the shank turns freely in the proximal cortex with the head against the bone as a fulcrum. A larger drill hole proximally serves the same purpose. On the other hand if threads are engaged in the proximal cortex the opposite fragment will be pushed away no matter how tightly the head may be against the bone. All carpenters know this when they wish to fasten boards tightly together.

After screws and plate are applied to the bone it is essential that adequate support and fixation of the extremity be provided as it is fallacious to assume that a plate alone, no matter how strong, will hold the fracture ends

tightly enough together to permit early exercise unless both peripheries are fixed. While the plate holds the upper periphery together during extension the margins of the opposite periphery are pulled apart. To illustrate if solid plates be substituted for hinges on a door it takes little force to show a crack on the opposite side. So in cases in which but one side is fixed with a plate alone a plaster cast controlling proximal and distal joints is necessary (Fig. 2).

This problem is encountered particularly in transverse or short oblique fractures of the femur and tibia due to the recumbent posture of the convalescent patient in whom it is so essential to maintain knee and ankle function, especially the former in which function is so easily lost. Because of the weight of the leg and the sag in the thigh or leg downward from the point of suspension by the plate on the upper periphery the margins of the lower periphery are separated in an inverted V throughout the width of the fracture ends. This is true no matter what manner of external fixation or support is used or how rigid the plate may be due to laxity of the posterior muscles which are beyond control of external fixation. Such a gap naturally predisposes to delayed union or to nonunion.

To meet this condition and secure an equally rigid fixation of both peripheries a long screw of the pull up or wood screw type placed obliquely to the axis of the plate through the upper surface of the proximal fragment, downward and backward across the fracture site through the cortex of the distal fragment will draw the fracture ends tightly together at the periphery opposite the plate and at the same time prevent any tendency to rotation of either fragment and also will materially lessen lateral movement (Fig. 3). This does not mean however that no external support is necessary that the limb is turned loose and the patient permitted to get up and walk. After suture of an abdominal wound, the patient is kept in bed a reasonable time for wound healing and so for bone healing there must be additional proper support and time allowance. However stable fixation allows almost immediate hip, knee and ankle function. In other words, encasement of the limb in plaster may and should

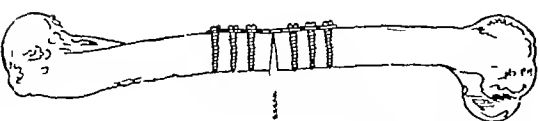


Fig 2 "Sag separation" of the periphery distal to the plate resulting from fixation with a plate on but one side of the bone

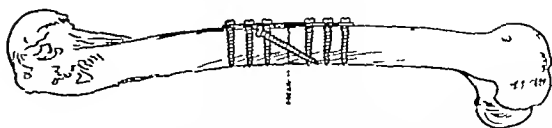


Fig 3 Stable approximation of distal periphery by engagement with transfixion screw placed obliquely through both fragments

be avoided if possible, while a plaster gutter with suspension in a Thomas half ring splint with the knee joint usually is quite sufficient. Such a procedure may be expected to shorten the period of disability to some 6 to 10 weeks as compared with the 12 to 20 weeks usually allotted.

The long oblique fracture offers yet another problem which, however, is more easily met through control of the distal periphery by complete transfixion of both cortices transversely by the use of pull up or wood type screws to draw the fragments together tightly. Two or more such screws may be so spaced that the fractured surfaces are held so firmly that joint function is admissible directly. In such instances, the addition of a plate is rarely necessary unless there is a complicating transverse fracture in the same field.

In short, bone as other tissue must be closely approximated and held so that it may regenerate promptly in the process of new cell growth. This emphasizes the essential in plating that close approximation of the bone ends must be obtained in all instances whether additional transfixion screws are applied or not. We see far too many cases of delayed union or non-unions because of improper application of a plate in which a gap of a $\frac{1}{32}$ or $\frac{1}{16}$ inch or more has been left.

My theme, however, is in principle, so details of varied technical applications of plates and screws will not be discussed. As I see it, the most important principle evolved is the chemical factor through the understanding of which it now becomes possible to apply direct fixation to fractures under conditions heretofore impossible. Compound fractures occurring in the presence of most severe trauma and infection with the outlook of bone union during the period of healing of an infected and traumatized wound may be expected in a very

high percentage of cases. In many instances it is possible now to plate and close a compound fracture after proper débridement and to expect wound healing as well as bone union as though a simple fracture were present.

During the past war direct fixation was forbidden because metals we then had were highly electroactive and increased the damage through deleterious bone changes so that non-union and even amputation resulted. Today we can feel safe in using metals for we now have available material that is passive, this fact has been proved in the recent past in the most severely traumatized and infected compound fractures occurring in the toll of automobile and airplane accidents as well as in industrial surgery. The same expectancy of greatly diminished nonunions and even amputations may now be expected in compound fractures occurring in war wounds.

SUMMARY

The first two factors, chemical and physical fitness, in the material for use in the treatment of fractures are supplied us by metallurgists, the third factor, application, must be mastered by each of us individually by an understanding of the mechanical principles involved, skillful technique, and that judgment acquired only through training and experience.

The introduction into bone surgery of material that is so tolerated as to cause no disturbance, opens fields we have not before known, but we must warn that it becomes a dangerous tool in the hands of those not qualified to use it. The same hesitancy and respect should be felt in operating to reduce fractures as in performing gastrectomies or in operating upon the brain. I say this because I believe that though the first two factors which have been mentioned are essential, the last—application—is the *sine qua non* of success.

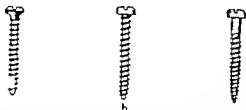


Fig. 1. Types of screw: a, dowel; b, wood-plain; c, wood-pull up. Note the obliquity and finer thread of the wood type screw.

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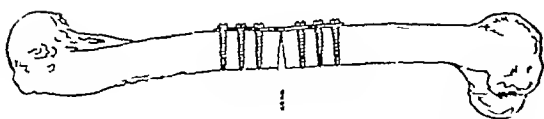


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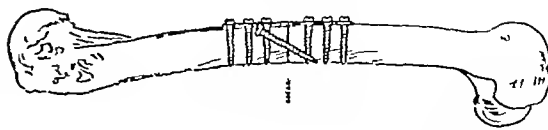


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RESULTS IN COMPOUND FRACTURES WITH OSTEOMYELITIS AS EXPERIENCED BY THE VETERANS ADMINISTRATION OVER THE PAST TWENTY YEARS

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IN modern warfare low velocity missiles cause the majority of compound fractures with their associated lacerations and contusions contaminated by clothing and skin resulting in gross infection after about 12 hours.

The standard treatment during and subsequent to the last war for compound fractures and osteomyelitis, according to the Surgeon General's Report of the Army for 1927 was as follows (a) proper splinting for transportation and first aid (b) debridement (c) skeletal traction and/or other immobilization (d) Carrell Dakin treatment or dichloramine T (e) surgery other than debridement as indicated (f) amputation and plastic repair (g) physical therapy

During the fiscal year of 1926 a summary of fractures and amputations of the long bones was studied by the Veterans Administration. The greatest number of fractures, 4,736 occurred in the humerus the next greatest in the femur. The greatest number of deaths, 1,060, or 35.03 per cent, resulted from fractures of the femur.

The tables covered a study of 22,954 fractures of the long bones over a period of 6 years. This group formed 5 per cent of the World War Veterans disabled to a compensable degree. The rating schedule used throughout the period under study based the degree of disability upon the average impairment of earning capacity resulting from injuries in civil occupations. On that date, 15,597 or 54 per cent of the fractures had reached a stationary level, which was reasonably certain to continue throughout the claimant's life. Thirty nine per cent of the total showed improvement and 7 per cent had retrogressed.

Fractures of the femur comprise the group of most serious injuries in the length of time required to reach a stationary level and in the high degree of disability. Amputation of the

TABLE I.—SURGEON GENERAL'S REPORT

	1927	No. cases	Per cent	No. days
Fractures following gunshot wounds—6 % returned to U. S. for treatment		5,377		
80.3 % compound		6,006		
Fractures, nonbattle, due to injuries, simple		30,559		
Total		70,847		
Percentage of injuries caused by low velocity missiles			70.41	
Loss of one or more extremities		4,403		
Associated joint involvement (ankylosis, flail joints, contractures, etc.)		4,970		
Percentage of total discharges for disability due to fractures		740	45.6	
Days lost due to fractures				5,125,220
Percent of all days lost due to all causes			39.3	
Average duration of treatment				5.30
Percentage of deaths as result of fractures in comparison to total			30	
No. deaths from fractures		757		
Total No. deaths		470		

TABLE II.—STUDY OF END-RESULTS IN FRACTURES OF LONG BONES BY THE U. S. PUBLIC HEALTH SERVICE AND U. S. VETERANS ADMINISTRATION 9-9-1926

	No. cases	Per cent
Simple fractures	4,519	16.69
Per cent under 30 years old		69.05
Per cent stationary		54
Per cent improved		39
Per cent retrogressed		7
Compound fractures	5,435	20.5
Complications—		
Osteomyelitis	4	33
Ankylosis, shortening, deformity, nonunion, flail joints, etc.		
Isch. involvement, etc.	6,505	
Total	4,538	

44 of these had history of total permanent, 46 of less than 100%

LIVINGSTON RESULTS IN COMPOUND FRACTURES WITH OSTEOMYELITIS 547

TABLE III—STUDY OF END-RESULTS IN FRACTURES OF LONG BONES BY THE U S PUBLIC HEALTH SERVICE AND U S VETERANS ADMINISTRATION, 1919-1926

	No cases	Per cent	Years to become stationary		Amputations	Less than 10 per cent	10-29 per cent	30-49 per cent	50-70 per cent	80-100 per cent
			Per cent 4 or more	Per cent 5+						
Femur	5 138	23	4	13	1 738	270	1 673	726	1 671	808
Tibia and fibula	4,485	20	5	23	1 140	764	1 968	1 27	244	116
Humerus	4,328	19	5	11	1 183	416	1 752	734	617	709
Radius and ulna	2 340	10	5	13	521	390	1 003	204	381	63

thigh contributed largely to the high rate of disability Table IV and the amputation report, by specific bone or bones, show the interval elapsing between the injury and the amputation Of the 4,179 amputations, 3,044 or 73 per cent were done within the first 15 days after injury The United States thus profited by the experience of the French and British by having mobile hospitals sufficiently equipped with surgeons and instruments to perform major surgery within the first 72 hours after injury

It should be noted that the average period of disablement is greatly in excess of the period recorded by observers for industrial fractures This is because the greater number of these fractures were compounded due to severe battle injuries Many of them later became septic with much destruction of tissue, including osteomyelitis, resulting in lasting deformity and much impairment of function Therefore, the character of these

fractures is of a far different type from those of civil life so the final results are not comparable

AMPUTATION REPORT

Phalangeometatarsal and transmetatarsal amputations These were infrequent but amputations in this area gave good function

Lisfranc's amputations at the transmetatarsal joint gave reasonably good function The dorsal flexors should be anchored to the ends of the bones to preserve dorsal flexion

Translarsal amputations Distal to Chopart's joint was preferable to Chopart's amputation, as proper balance of the dorsal and plantar flexors of the foot was better preserved

Chopart's amputations resulted in poor function Plastic repair did not usually improve the function and reamputation was often necessary Equinus too short for proper prosthesis

Pirogoff's amputation Displacement of the remaining portion of the calcaneus was common The total end bearing stump, following the Syme's amputation, is quite as satisfactory

Syme's amputation The chief advantages in the Syme amputation were that it was total end bearing and the length of the limb was approximately preserved so the patient could get about without his prosthesis This amputation has been found highly satisfactory and must be considered as a site of election

Leg, lower third All cases observed as a reamputation because of poor vascularity and complications

Amputation of leg (calf) was considered in the Surgeon General's Report, 1927, as the ideal site for anatomical and prosthetic reasons Subsequent experience in the Veterans Administration has shown a high percentage of neuromas, ulcers, painful stumps, and painful weight bearing surfaces Reamputation (Gritti-Stokes or thigh) has been found the only answer to the problem in many of these cases

TABLE IV—STUDY OF END-RESULTS IN FRACTURES OF LONG BONES BY THE U S PUBLIC HEALTH SERVICE AND U S VETERANS ADMINISTRATION, 1919-1926

AMPUTATIONS

	Interval elapsing between injury and amputation				Death	Total
	Days 1-31	Months 2-12	Over 1 year	Over 4 years		
Thigh	1,374	354	14	76	76	1 818
Leg	860	250	25	49	49	1 190
Arm	641	44	3	39	39	727
Forearm	391	7	3	23	23	444
Total	3 66	681	45	187	187	4 170

Thigh Knee joint and transcondylar amputations were found satisfactory. Gritti-Stokes amputations required a high percentage of reamputations (Surgeon General's Report, 97). Subsequent experience points with favor to this operation provided the patella has firmly adhered to the femur and is well placed. Amputations at various levels from high transcondylar to inches below the lesser trochanter have proved satisfactory. Amputation through the neck of the femur has been found preferable to disarticulation at the hip joint.

Hand Cases in which only a débridement with heroic efforts to save all those possible pedicle transplants, and plastic repairs offered the most desirable results. Transcarpal amputation was found preferable to amputation at the wrist. Wrist joint amputation was preferable to any higher plane. The club-like stump eliminated much apparatus in the prosthetic hand.

Forearm Amputation of the forearm should be done as low as possible. The importance of preserving supination and pronation warrants careful treatment of the periosteum to prevent bridging. A forearm stump should not be sacrificed to overcome painful scars, ulcers, etc., but plastic measures should be used on the soft structures.

Arm Transarticular and transcondylar amputations have not proved satisfactory from the standpoint of prosthetics. Above this level all possible bone length should be saved. Short arm stumps may be improved so far as leverage is concerned by severing or raising the insertions of the pectoralis muscles, the latissimus dorsi, and teres major. The head of the humerus should always be saved if possible, to preserve the contour of the shoulder.

CONCLUSIONS

1. Eighty and thirty-one hundredths per cent of battle fractures were compound, nearly one-half of all discharges, nearly one-third of all days lost and one-fifth of all deaths were the result of fractures.

2. About one-half of all compound fractures required more than 5 years before becoming stationary.

3. The relatively large number of late amputations indicates early surgery is advisable and that mobile hospitals should be equipped for major surgery.

4. Seven years after World War I the majority of compound fracture cases were compensable from 10 per cent to 50 per cent, with a smaller but still large number from 50 per cent to 100 per cent.

5. In 1930 there were about 10,000 old and recent cases of osteomyelitis in the Veterans Administration due to all causes. From the treatment of these cases the following conclusions may be drawn:

a. In cases of compound fractures early anatomical alignment should be accomplished by open or closed manipulation with maintenance by external or internal fixation. Hardware, such as Parham bands, Lane or Sherman plates, screws, etc., may be applied at the time of the débridement, the presence of infection not being considered a contraindication.

b. A thorough but careful early débridement is advisable.

c. Antigas and antitetanus serum should be administered prophylactically in all cases. Only too often is antigas serum omitted. The prophylactic use of these serums is again advised before delayed surgery is attempted.

d. Lacerations should be sutured early with interrupted silk sutures which may be easily removed if necessary.

e. The early intravenous use of blood serum or plasma is a great aid in the treatment of shock.

f. The use of the sulfonamides by mouth and locally is strongly recommended.

g. Sequestrectomy in chronic osteomyelitis should be thorough and include areas of osteosclerosis. In a slowly but steadily progressing molecular necrosis wide excision to areas obtaining their blood supply from collateral circulation or amputation is indicated. Osteomyelitis of the lower third of the tibia, especially if involving the ankle joint, usually results in amputation and this is recommended early.

h. Syme's and Gritti-Stokes amputations are amputations of election. Amputation at the calf is usually to be condemned. A mid thigh or Gritti-Stokes amputation is preferable.

i. Maggot therapy, although condemned by many, is an effective treatment for osteomyelitis, as is the Orr method.

j. Local irrigating solutions, antiseptics, and pastes of various kinds have not proved effective in the treatment of osteomyelitis.

PRECANCEROUS LESIONS

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BY definition, a precancerous lesion is one in which, statistically, the tissue is more likely to become invasive and metastasizing than is tissue involved in other, non-precancerous types of change. Since I have been asked to discuss precancerous lesions, and the exact phase of the topic was not specified, I infer that considerable latitude has been left to my judgment. I have chosen, accordingly, to discuss a view in which I am particularly interested and toward which all the investigative energies of my group have been directed for a number of years. It would be redundant to present before this assembly the conventional statements regarding the changes which are considered to be precancerous. It is common knowledge that oral and vulval leucoplasia tend to become neoplastic, and that keratoses of the skin are very likely to do so. Less well known is the fact that only certain forms of mammary epithelial hyperplasia are prone to become malignant, and that the precancerous alterations of the gastric mucosa are not well understood. To obtain a better comprehension of the nature of the precancerous lesions, it is desirable to ascertain, from the study of those which have been proved, some common factor. Then, by the methods of modern scientific investigation, it should be possible to establish the means by which this common factor can be regularly induced in man and animals. Once such a mechanism were established, rational prophylaxis would follow logically, and only by the development of prophylactic methods are we likely to advance materially the cure of cancer, barring, of course, the occurrence of some major technical development.

What, then, is the common factor to be discerned in those changes which are known to tend to become neoplastic? In the skin, in the oral cavity, as well as in the hematopoietic apparatus, this common factor appears to be a chronic irritative one, but actually is probably an atrophy due to some mechanism which prevents the normal life and reproduction of the affected cells. Similarly, atrophy may well play a rôle, although as yet unproved, in the precancerous lesions of the genital organs, notably the breast, the uterus,

and the prostate. At least one is safe in stating that cancer of these organs occurs at a time when their epithelium becomes functionally inactive, and when the metabolism of the specific chemicals, the sex hormones, which control their activity, becomes gravely altered. It is fair to assume, then, from the evidence, that the overgrowth which, when uncontrolled, is neoplastic, is in some instances a pathological response to the cause of the primary atrophic lesion. Obviously, then, it is desirable to establish clearly the cause of tissue atrophy in general.

In Table I are presented recognized examples of cancer which is known to follow the appearance of an atrophic process. Among these certain ones stand out as disorders without any known etiology. In at least three types, however, one can advance rather strongly suggestive evidence concerning causation. These types affect the skin, the liver, and the hematopoietic apparatus.

The evidence concerning the atrophic and precancerous lesions of the skin is clear, and needs little further discussion, since methods of measuring the function of its cells are not well established. As concerns the blood-forming organ, somewhat more information is available. From the observations of Hunter and Mallory, to which we have been able to add confirmatory evidence (3), it is clear that exposure to compounds of a known chemical structure, notably benzene, will cause, first, an atrophy and later the malignant overgrowth which we call leucemia. These changes are illustrated in Figs 1 and 2.

Liver cancer, however, provides a particularly useful experimental tool, since in the animal it can be produced regularly under certain circumstances by a compound of known chemical constitution. Furthermore, in the animal sufficient

TABLE I.—PRECANCEROUS CHANGES

- 1 Skin
 - A Keratoses of the atrophic skin
 - B Xeroderma pigmentosa (atrophy)
 - C Radiation dermatitis (atrophy)
 - D Burn scars and lupus (atrophy)
 - E Arsenic dermatitis (atrophy)
- 2 Kraurosis vulvae (atrophy)
- 3 Plummer Vinson disease (atrophy)
- 4 Thyroid cancer after hypothyroidism
- 5 Cancer in undescended atrophic testicle
- 6 Cancer of liver on cirrhosis
- 7 Leucemia on aplastic anemia



Fig.

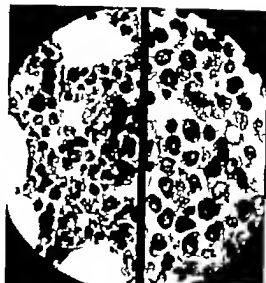


Fig. 2.

quantities of liver tissue for analysis can be made available easily. It is desirable, then, to examine the facts in order to ascertain to what extent liver cancer represents a primary atrophy followed by a malignant overgrowth, and how far experimental liver cancer is analogous to liver cancer in man. Kinosita has proved that the feeding of dimethylaminobenzene (butter yellow) to rats taking a diet of rice will produce regularly hepatic cirrhosis followed by hepatic cancer. Cirrhosis is clearly an atrophic process, and in this instance is precancerous.

How far can the analogy be drawn between this type of experimental neoplasms and liver cancer in man? Some points of similarity certainly exist. Human liver cancer tends to occur on a basis of cirrhosis, a point clearly proved by a recent communication from South Africa. In a very large series of patients with hepatic malignant neoplasms cirrhosis was always present.

What, then, is the nature of cirrhosis? Clearly it is a process which involves damage or death of normal liver cells and their replacement by regenerative tissue. How, then, can this basic process of atrophy be induced, and why should the regenerative effort of the liver give rise to cancer? The experiment of the Japanese workers previously described provided a method for the analysis of these problems. Obviously it was desirable to ascertain how the combination of a rice diet and the administration of butter yellow operated to produce the primary cellular damage marked by

atrophy. Kensler and Segura, in my laboratory immediately attacked the problem. First they proved that the experiments described by the Japanese could be repeated regularly. Next the diets were analyzed to see what factor in them was lacking and was supplied by yeast. Third, the effect of butter yellow feeding on liver cells was examined and fourth, the compounds into which butter yellow is broken down in the animal were isolated and identified. We proved that at least two factors were lacking in the diet which rendered the animals susceptible to liver cancer following the ingestion of butter yellow. The effect of the feeding of this carcinogen was found to be a poisoning of the activity in the liver cells of certain enzyme systems required for the respiration and metabolic function of normal cells. Here, then, was an explanation of the atrophic or precancerous process. Next the particular breakdown product of the chemical carcinogen which interfered with the respiration of normal cells was identified. Finally certain evidence was obtained as to how this injurious effect was exerted. The fact became clear that the cancer-producing chemical induced atrophy of liver cells by competing successfully for the protein component of the cells without which their enzyme systems could not operate. If the efforts of the cancer-producing chemical to steal the enzyme protein could be directed into innocuous channels it would be possible to prevent the cancer-producing effect.

Why, then, does malignant overgrowth take place? All the details of this mechanism are, of course, not as yet worked out. One fact does appear clear, however. The cancer recurs and grows in the face of a milieu which is incompatible with the life and growth of normal cells. One would infer, therefore, that the cancer cell is malignant because it has developed some new way of life which renders it insusceptible to damage by the chemical compound employed in the experiment and concurrently immune to normal growth restraint. Were this the case, the respiration of normal liver cells and not that of liver cancer cells. This is the case. Furthermore, this observation should be confirmable by another technique in another laboratory. Robert Chambers, at New York University, has confirmed the observation in tissue culture. Here, again, a concentration of a toxic breakdown product of butter yellow which will kill normal rat liver cells has no effect upon the growth and multiplication of liver cancer cells.

It may be argued that this type of fundamental work has no bearing on the problem of cancer in man. This may be the case, but if, as we assume from the results of the experiments described, the cancer cell is different in its respiratory mechanism from normal cells, it is not impossible that the future will provide us with effective chemotherapeutic agents.

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THE RÔLE OF THE RADIOLOGIST IN THE CANCER CLINIC

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DURING the past 25 years there has been a considerable advance in our knowledge of and our interest in, the diagnosis and control of cancer. Early in this development it was recognized that some methods of attacking the problems should be devised which would bring together those physicians and scientists interested in the problem and which would permit the grouping of patients suffering from this disease for study and follow-up. In an attempt to solve this problem two plans have been developed which have received general acceptance throughout the world, namely the cancer hospital, and the tumor clinic—both of these methods have advantages and disadvantages.

The cancer hospital is a considerably older development in point of time than the tumor clinic and in general it may be said that this method of approach has been more successful in fundamental research and in adding to our knowledge of the whole problem than has the tumor clinic. On the other hand, the tumor clinic has been outstanding in the therapeutic field and seems to be a better method of bringing a knowledge of the disease to physicians in general.

The cure of cancer is still largely a surgical problem. Irradiation being reserved for those patients who have passed the stage in which surgery can reasonably be expected to effect a cure or in whom for some reason surgery is contra-indicated. If this general statement is accepted, the treatment of curable cancer then becomes largely a question of surgical skill. No surgeon is equally skillful in operating upon all parts of the human body; surgeons have recognized this fact, and specialization takes place along anatomical lines rather than by disease. The surgeon working in a cancer hospital must of necessity confine himself almost wholly to the treatment of cancer in some particular anatomical location and it is questionable whether or not a surgeon would receive sufficient material for his proper development in a cancer hospital except in a few very large centers of population. As a matter of fact most cancer hospitals do not attempt to

treat cancer in all of its anatomical manifestations, as for example tumors of the brain, lungs, and gastrointestinal tract. In most of the cancer hospitals today surgery plays a minor rôle the major effort being devoted to research and radiation therapy.

The tumor clinic on the other hand, offers an excellent opportunity for the development of surgical treatment in all fields of cancer. The operating surgeon in these clinics occupies an important position on the surgical staff of a large general hospital and the material which he has for study is ample. Another advantage of the tumor clinic is that its work is brought directly to the staff of the general hospital and to the practicing physicians of the community. In this way these physicians obtain first hand knowledge of the problem, rather than obtaining such information from occasional visits to large cancer centers or through the literature.

In so far as I am able to determine the first tumor clinic, as it is known today was established at the Massachusetts General Hospital in 1925 and grew out of a consultation service developed by the department of radiology dating back to 1919 when the first consultant was appointed to this clinic. At the Clinical Congress of the American College of Surgeons held in Philadelphia in 1930 Dr. Robert B. Greenough read a paper in which he described the work of the tumor clinic and told of its developments. The advantages of the clinic as stated by him at that time were as follows:

The work in cancer cases is placed in the hands of those members of the staff who are most interested in that subject.

Opportunity is given by consultation with representatives of the clinical, pathological, and radiotherapeutic departments for mutual instruction and increase of knowledge of the disease and its treatment.

3. A definite rational plan of treatment can be determined for each individual case, after consultation and the results can be checked and discussed, by the group, in the subsequent follow-up.

4. Concentration of the hospital material permits greater experience and more productive work.

5. The standards of the hospital for efficient diagnosis and treatment of cancer are inevitably raised, and the educational effort extends beyond the hospital to medical students and to physicians in general practice in the immediate vicinity.

From the Massachusetts General Hospital.
Presented at the Cancer Symposium before the Clinical Congress of the American College of Surgeons, Boston, November 7-

6 The additional expense to the hospital involved in the maintenance of the tumor clinic amounts only to about \$3000 00 a year

This report received the favorable attention of the College and the development of similar clinics in other centers has been largely due to their effort

The personnel of a tumor clinic should consist of a surgeon, or better, a group of surgeons trained and interested in the treatment of cancer, a radiologist, or group of radiologists, similarly trained and interested in the problem, an internist, a pathologist, a social service worker, and one or more clerks and nurses. It is of the greatest importance that the physicians composing the staff be on a somewhat equal footing. The clinic should not be dominated by either the surgeon, the radiologist, the pathologist, or the clinician. The executive head of the clinic should be chosen for his personal qualifications and for his interests in the problem as a whole, rather than because of his position in any one field of medicine.

At the present time, at the Massachusetts General Hospital, the direction of the tumor clinic is in the hands of a committee which represents surgery, medicine, radiology, and pathology—the chairman of the committee being the chief surgeon. All appointments to the staff are approved by this committee on the recommendation of the chief of the service involved.

The tumor clinic acts primarily as a consulting and follow-up service. The treatment, whether it be surgical, medical, or radiological, is under the control of the chief of the general medical, surgical, or radiological service. Much of this treatment is handled by special assignment by members of the tumor clinic regarding treatment receives serious consideration. It has been found advantageous to carry on a certain amount of minor surgery in the tumor clinic itself, such as the taking of specimens for biopsy or the removal of small superficial lesions. It has also been found desirable to hold the clinic in close contact with the x-ray therapeutic department, this encourages the follow-up of patients and makes available to the department of radiology immediate surgical or medical consultations. Patients referred to the clinic for consultation are first seen by the resident surgeon or radiologist assigned to the department and are referred to the specialty in which the location of their disease places them. Whether or not other specialists are asked to see the patient will depend largely upon the possibility of surgical, medical, or radiation therapy. The opinions given to the service referring the patients is that of the clinic as a whole, rather

than of a single individual in most cases and in all controversial cases. Since the treatment of cancer in most cases at the present time is either surgical or radiological the selection of cases for these procedures is of great importance. In arriving at a decision many factors should be considered, most important of which are the stage of the disease, histology of the tumor, the age and condition of the patient, the location of the tumor, and the chance of cure or relief by the various methods of treatment. It is not sufficient for the surgeon to state in a given case that he believes the disease is curable by surgery. He must also state the amount of permanent damage resulting from the operation and the risk, the same is true regarding the opinion of the radiologist. If, in the opinion of the surgeon, the tumor cannot be removed completely, or if the operative risk is too great, irradiation should be considered. An attempt to cure by irradiation usually results in considerable discomfort for the patient and in permanent damage to tissue in the radiated field. It should not be undertaken unless there is a reasonable chance of cure. Palliative treatment, on the other hand, will often control the disease for a considerable period of time and relieve suffering. It is important that this distinction be recognized and that the treatment be not too prolonged or severe with an incurable patient.

The selection of the kind of irradiation in a given case will depend largely upon the location and character of the tumor. The use of radium in our clinic has decreased rapidly during recent years and is now largely confined to treatment within accessible body cavities, an excellent example of which is the uterine cervix. It may be used to destroy a residual tumor after irradiation with x-ray, but this field of its use is definitely limited, needles or seeds should not be inserted where there is danger of infection. Since the use of radium at the present time requires, in most cases, a surgical operation we have found it more satisfactory to allow the surgeon to carry out the entire procedure rather than to call in a radiation therapist to apply the radium. The application of radium as used today is relatively simple and the surgeon can master the radiation technique with much greater ease than the radiologist can the surgical technique. The use of irradiation with x-ray, either preceding or following a surgical procedure, also has, in our opinion, a limited field of usage, although it has in the past been used extensively.

Postoperative irradiation, rarely if ever, cures a patient who was incurable by surgery in the beginning, although it may prolong the period in

which the patient is free of recurrence. Nor will preoperative irradiation make an inoperable case operable. The feeling prevalent among some surgeons that, if the operation fails, irradiation may be used to effect a cure should be discouraged. An operation should not be attempted unless there is reasonable chance of cure. These patients are better handled by irradiation alone. Post-operative irradiation should be used in those cases in which after operation, it is found necessary to change the original diagnosis. In those cases in which the surgeon realizes at the time of operation that he is unable to remove the tumor completely or in which histological examination of the tumor following operation shows the disease to be of high degree of malignancy. In this latter group particularly if the tumor is known to be radiosensitive, preoperative irradiation in rather small doses may be found to be of value.

It has been our experience that the best results are obtained when the therapeutic procedure is planned after consultation between the surgeon and the radiologist. The procedure then is carried out as a joint undertaking in which either of the consultants may proceed independently calling the other in for consultation when his method has failed.

The tumor clinic affords an excellent opportunity for free discussion of the therapeutic procedure to be adopted in individual cases, and the end-results made available by the follow-up system allows comparison of results.

Perhaps it may seem to you that I have wandered considerably from the subject which I was asked to discuss, namely "The Role of the Radiologist in the Cancer Clinic," but to me it seemed necessary to state the fundamental principles involved in the management of a cancer clinic before attempting to answer the question—which, after all, can be stated in a few words.

The position of the radiologist in the tumor or cancer clinic is that of any other members of the professional staff—that of a consultant.

The physician in charge of the patient will make the final decision after he has received the advice of the various specialists connected with the clinic and the treatment accepted will be carried out by the physician or service to which the patient is referred. The physician should accept full responsibility once the patient is placed in his hands. In other words, if after consultation and discussion surgical treatment is believed to be the method of choice, the responsibility should be in the hands of the surgeon in charge.

If on the other hand, irradiation is considered the method of choice, the radiologist is responsible for its administration and for the care of the patient during the time in which it is being administered.

Any attempt to direct the surgical procedure by the radiologist or the radiological procedure by the surgeon can result only in confusion.

Finally the position of any specialist in the clinic depends to a large extent upon his ability and his willingness to serve.

RADICAL SURGICAL TREATMENT FOR CARCINOMA OF THE CARDIAC END OF THE STOMACH

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IN a recent communication I called attention to the fact that the renewed interest in the surgical treatment of cancer of the thoracic esophagus has centered attention on a problem in abdominal surgery which has received little recognition in the past. I refer to carcinoma of the cardiac end of the stomach. In spite of rapid advances in the diagnostic methods of roentgenography, esophagoscopy and gastroscopy, and improvement in surgical technique, surprisingly few attempts have been made to extirpate cancer of the cardiac end of the stomach. The paucity of reports in surgical literature of this subject is noteworthy. Sustained interest in a subject such as the surgical treatment of cancer must be maintained by repeated and continued reports of encouraging progress in the fight against this disease. With this in mind, I would like to summarize my experience with the surgical treatment of carcinoma of the cardia to date, enlarging somewhat on a few of the details reported in the paper already referred to.

The cardia of the stomach may present considerable variation in size, shape, and position. In most individuals, the terminal one half to three-quarters of an inch of esophagus lined by squamous epithelium, occupies an intra-abdominal position just below the diaphragm. It is known as the cardiac antrum. Operative experience has shown that the junction between esophagus and stomach is usually sharply defined and is indicated by an indentation on the greater curvature side, the incisura cardiaca. At the point of union with the esophagus, the musculature and mucous membrane of the stomach are thickened to form the incisura cardiaca. At the point of union with the esophagus, the musculature and mucous membrane of the stomach are thickened to form the incisura cardiaca. At the point of union with the esophagus, the musculature and mucous membrane of the stomach are thickened to form the incisura cardiaca.

I from the Surgical Service of the Mount Sinai Hospital New York City N Y
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curvature side to include the upper part of the fundus. The cardiac orifice is usually situated at the level of the eleventh thoracic vertebra behind, and the seventh left chondrosternal junction in front. At the esophagocardiac junction, there is a sharp change in the histological characteristics of the mucous membrane. Above, the mucosa is of the squamous cell variety, while below, it assumes columnar characteristics. It is important to remember therefore that carcinomas originating in adenocarcinoma in contradistinction to the squamous cell tumors arising in the esophagus. An adenocarcinoma of the cardia may grow upward along the lower esophagus for a considerable distance. The biopsy specimen obtained by esophagoscopy will always indicate the origin of the tumor. It is important to stress this point because on numerous occasions I have heard the statement made that the finding of an adenocarcinoma in the lower esophagus often indicated malignant degeneration in misplaced gastric mucosa. This I believe to be completely inaccurate because a large operative experience has proved that every instance of adenocarcinoma of the esophagus has originated in the cardia or upper stomach.

It is important to stress what direction the lymph node spread may take from cancers of the upper end of the stomach. In general, the initial spread is toward the nodes in the gastrohepatic omentum and those located along the greater curvature near the incisura. Involvement of the peripancreatic nodes may occur late in the disease. In general, it may be said that adenocarcinomas arising at the cardia spread peripherally below the diaphragm toward the gastrohepatic or gastrocolic lymph nodes, depending in part, upon the location of the tumor with respect to the lesser or greater curvatures. Extension above the diaphragm to the nodes in the posterior mediastinum occurs not infrequently. Early metastatic involvement of the liver is a frequent finding. This invasion of the gastric veins by tumor tissue with extension to the portal system. As with carcinoma elsewhere, the prognosis is materially altered when gross node involvement is demonstrated.

TABLE I.—ESSENTIAL DETAILS OF THE CASES REPORTED IN THIS PAPER

Patient's Age	Approximate duration of symptoms	Location of tumor	Biopsy	Operation	Postoperative complications	Follow up	Remarks
R. Z. M. 63	5 mos.	40	Adenocarcinoma	10-13-30 Abdominal exploration, inoperable	None	Dead of disease months later	
L. S. M. 56	mos.	30	Adenocarcinoma	10-29-30 Thoracic exploration, inoperable, gastrostomy performed	Falsely diagnosing pneumonia at autopsy	Dead on third day	At present time, would explore abdomen first to determine operability
M. M. M. 60	1 1/2	40	Adenocarcinoma	10-6-30 Trans-thoracic exploration, inoperable Gastrostomy performed	None	Dead soon later	At present time, would explore abdomen first to determine operability
S. R. F. 58	1 1/2	35	Adenocarcinoma	7-11-30 Abdominal exploration, trans-thoracic, resection with omentum	None	Well 18 months post-operative	One lymph node showed involvement
A. M. M. 60	About 1 mos.	40	Adenocarcinoma	6-6-30 Abdominal exploration, Trans-thoracic resection with omentum	None	Well 18 months post-operative	No involved nodes found
C. L. M. 60	mos.	30	Adenocarcinoma	1-7-30 Abdominal exploration, inoperable Spewack gastrostomy	None	Dead of disease soon later	
H. S. M. 67	mos.	40	Adenocarcinoma	6-21-30 Abdominal exploration, inoperable	None	Dead soon later of disease	
S. L. M. 65	10 wks.	35	Adenocarcinoma	7-24-30 Abdominal exploration, inoperable	None	Dead soon later of disease	
G. K. J.	mos.	35	Adenocarcinoma	10-17-30 Abdominal exploration, inoperable Jejunum gastrostomy	None	Dead soon later of disease	
I. G. F.	8 wks.	30	Adenocarcinoma	6-28-30 Abdominal exploration, inoperable Jejunum gastrostomy	None	Dead soon later of disease	
J. G. M. 46	6 mos.	40	Adenocarcinoma	7-10-31 Abdominal exploration Trans-thoracic resection and omentum	None	Well soon post-operative	Associated lymph nodes removed with tumor showed involvement
H. C. M. 66		40	Adenocarcinoma	7-11-31 Abdominal exploration Trans-thoracic resection and omentum	Gastrostomy performed on 10-3 day Autopsy	Dead suddenly on 10-3 day	Length of history and operability not worthy
I. L. M. 51	1 wks.	40	Adenocarcinoma	7-2-31 Abdominal exploration, inoperable	None	Still alive	
J. A. M. 49	mos.	30	Adenocarcinoma	10-30 Trans-thoracic resection and omentum	Cephalexin on 10-30 Autopsy	Dead on 3rd day	Lymph nodes showed involvement
M. R. F. 70	mos.	30	Adenocarcinoma	7-24-31 Abdominal exploration inoperable Jejunum gastrostomy	None	Dead of disease soon later	
J. R. M. 62	mos.	40	Adenocarcinoma	10-3-31 Abdominal exploration, inoperable Jejunum gastrostomy	None	Dead of disease soon later	
W. C. M.	mos.	30	Adenocarcinoma	10-17-31 Abdominal exploration, chest exploration, inoperable	None	Dead of disease soon later	Extensive metastatic node involvement
C. D. M. 56	mos.	30	Adenocarcinoma	7-1-31 Jejunum gastrostomy 7-19-31 Chest exploration, inoperable	Post-operative pneumonia	Dead soon later	
L. R. F.	10 wks.	30	Adenocarcinoma	8-7-30 Trans-thoracic resection and omentum	Became comatose on 3rd day	Dead on 4th day	Autopsy essentially negative
H. H. M. 49	1 1/2	30	Adenocarcinoma	6-20-30 Trans-thoracic resection and omentum 7-9-30 Right thoracotomy for pyopneumothorax	Developed ruptured lung a hernia of right lung	Lived for 15 mos. Dead of extensive retroperitoneal metastases	Resected specimen showed extensive node involvement

RADICAL SURGERY FOR CARCINOMA OF CARDIA
TABLE I—ESSENTIAL DETAILS OF THE CASES REPORTED IN THIS PAPER—Continued

Patient Sex Age	Approx imate duration of symptoms	Loca tion of tumor cm	Biopsy	Operation	Postoperative complications	Follow up	Remarks
H M 30	6 wks	40	Hodgkin's disease of cardia	4-12-41 Abdominal exploration trans thoracic resection and anastomosis	None	Doing well 7 months postoperative	This case is included in series for obvious reasons
M F 61	5 mos	40	Negative biopsy	5-14-41 Exploratory laparotomy inopera ble	Several severe gastric hemor rhages	Still alive	
M B 57	3 mos	40	Adeno- carcinoma of cardia and lower esophagus	5-21-41 Exploratory laparotomy trans thoracic resection and esophagogastric anastomosis	Mediastinal abscess and peritonitis	Died on 9th day postoperative	Leakage from small perforation of esoph agus at site of operative injury Suture line intact
J G 57	3 mos	40	Adeno- carci noma	6-4-41 Abdominal exploration inoperable	None	Alive	
R M 55	4 wks	30	Adeno- carci noma	8-6-41 Abdominal exploration adherent to pancreas metastases to diaphragm	None	Alive	

ble at operation. However, this should not deter the surgeon from carrying out radical extirpation of the growth and all the associated lymph nodes. Follow-up studies have demonstrated that a not inconsiderable proportion of such cases have survived the 5 year period. Metastatic involvement of the liver immediately classifies the case as inoperable. I do not believe that any patient with a resectable growth associated with hepatic involvement should be subjected to so extensive a procedure as a palliative measure.

The symptoms produced by a neoplasm at the cardia of the stomach will, in large part, depend upon the exact site of origin of the tumor and the direction of this growth. Cancers arising at the cardiac orifice quickly interfere with the act of deglutition and produce symptoms of lower sub-sternal pain, especially on swallowing. These tumors usually extend upward to involve the lower esophagus. On the other hand, a tumor originating on the greater curvature side of the cardia, in the so called silent area of the stomach, may produce no symptoms whatever until the growth has extended into the orifice itself. By the time dysphagia is noted by the patient, the carcinoma may very well have reached the inoperable stage. This type of case has been a factor in lending discouragement to active surgical treatment for cancers of the upper end of the stomach. However, it is important to emphasize that many of these patients may have persistent indigestion which resists medical treatment or that there may be an unexplained loss of weight. In such circumstances, it is imperative that the physician avail himself of every diagnostic method to demonstrate the presence of a tumor in this region. In

general, the symptoms will depend upon the proximity of the tumor to the stream of swallowed food and the size of the growth with respect to diminution of the caliber of the cardiac orifice or lower esophagus.

In a number of instances, operative exploration has demonstrated extension of the growth beyond the wall of the stomach to the posterior parietes or to the body of the pancreas. These patients have complained of back pain usually located to the left of the midline at the level of the eleventh or twelfth thoracic vertebra. This symptom has generally occurred late in the disease. A careful evaluation of the symptom of persistent back pain is of considerable importance in estimating probable operability.

An analysis of the cases reported in this paper indicates that loss of weight does not reach the extremes frequently seen in operable squamous cell carcinomas of the esophagus and that when great weight loss has occurred, the tumor, in all probability, will be found to be inoperable by reason of extensive node involvement or extension to the liver. The question of weight loss, therefore, is of considerable importance to the surgeon in helping him to estimate operability.

Malignant degeneration of a pre-existing benign ulcer at the cardia brings up the ever recurring debatable problem. There were 3 instances in this series of a long-standing ulcer history with relief of symptoms by the usual medical therapy, and, in one instance, the x-ray films, fortunately preserved, taken 10 years ago, showed a small penetrating ulcer at the lesser curvature side of the cardia. In the latter case, symptoms became more persistent in the last few months and did not re-

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Patient Sex Age	Approximate duration of symptoms	Location of tumor on	Biopsy	Operation	Postoperative complications	Follow up	Remarks
H. E. M.	3 mos	20	Adeno- carcinoma	11-2-30 Abdominal exploration, inoperable	None	Died of disease months later	
L. S. M. 34	mos	20	Adeno- carcinoma	10-10-30 Thoracic exploration, inoperable, gastrostomy performed	Yeastlike pneumonia at autopsy	Died on third day	At present time, would explore abdomen first to determine operability
M. M. M. 60	wtz	20	Adeno- carcinoma	10-6-30 Trans-thoracic exploration, inoperable Gastrostomy performed	None	Died mos later	At present time, would explore abdomen first to determine operability
S. R. F. 35	12	13	Adeno- carcinoma	7-12-30 Abdominal exploration, trans-thoracic resection with omentum	None	Well 23 months post-operative	One lymph node showed involvement
A. M. M. 60	About mos	20	Adeno- carcinoma	6-6-30 Abdominal exploration Trans-thoracic resection with omentum	None	Well 17 months post-operative	No involved nodes found
C. L. M. 60	mos	20	Adeno- carcinoma	2-7-30 Abdominal exploration, inoperable Gastrostomy	None	Died of disease mos later	
H. S. M. 47	mos	20	Adeno- carcinoma	6-26-30 Abdominal exploration, inoperable	None	Died mos later of disease	
S. L. M. 43	10 wks	13	Adeno- carcinoma	1-26-30 Abdominal exploration, inoperable	None	Died mos later of disease	
G. E. F. 33	mos	16	Adeno- carcinoma	10-7-30 Abdominal exploration, inoperable Jejuney gastrostomy	None	Died mos later of disease	
I. G. F.	wtz	20	Adeno- carcinoma	6-26-30 Abdominal exploration, inoperable Jejuney gastrostomy	None	Died mos later of disease	
J. G. M. 46	mos	20	Adeno- carcinoma	7-14-30 Abdominal exploration Trans-thoracic resection with omentum	None	Well 8 mos post-operative	Uninvolved lymph nodes removed with tumor showed involvement
H. C. M. 60		20	Adeno- carcinoma	4-1-32 Abdominal exploration Trans-thoracic resection and omentum	Cervical node seen on 14th day Autopsy	Died suddenly on 14th day	Length of history and operability note worthy
I. L. M.		20	Adeno- carcinoma	7-7-30 Abdominal exploration, inoperable	None	Still alive	
J. A. M. 49	mos	20	Adeno- carcinoma	10-29 Trans-thoracic resection and omentum	Cervical node taken Autopsy	Died on 3rd day	Lymph nodes showed involvement
M. B. F. 70	mos	20	Adeno- carcinoma	10-26 Abdominal exploration inoperable Jejuney gastrostomy	None	Died of disease mos later	
J. S. M. 61	mos	20	Adeno- carcinoma	10-7-30 Abdominal exploration, inoperable Jejuney gastrostomy	None	Died of disease mos later	
W. C. M.	mos	20	Adeno- carcinoma	10-9-30 Abdominal exploration cholecystectomy, inoperable	None	Died of disease mos later	Extensive metastatic node involvement
C. D. M. 50	mos	10	Adeno- carcinoma	7-1-31 Jejuney gastrostomy 4-10-31 Chest exploration, inoperable	Postoperative pneumonia	Died mos later	
L. E. F.	12	20	Adeno- carcinoma	8-3-30 Trans-thoracic resection and omentum	Bleeding from chest on 3rd day	Died on 4th day	Autopsy essentially negative
B. H. M. 40	wtz	20	Adeno- carcinoma	6-20-30 Trans-thoracic resection and omentum 7-1-30 Right thoracotomy for pyothorax-thorax	Developed ruptured lung abscess of right lung	Lived for 16 mos Died of extensive metastatic involvement	Extensive metastatic node involvement

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Patient Sex Age	Approx imate duration of symptoms	Loca tion of tumor cm	Biopsy	Operation	Postoperative complications	Follow up	Remarks
H H M 39	6 wks	40	Hodgkin's disease of cardia	4-12-41 Abdominal exploration trans- thoracic resection and anastomosis	None	Doing well 7 months postoperative	This case is included in series for obvious reasons
M F M 61	5 mos	40	Negative biopsy	5-14-41 Exploratory laparotomy inopera- ble	Several severe gastric hemor- rhages	Still alive	
M B M 57	3 mos	40	Adeno- carcinoma of cardia and lower esophagus	5-21-41 Exploratory laparotomy trans- thoracic resection and esophagogastric anastomosis	Mediastinal abscess and peritonitis	Died on 6th day postoperative	Leakage from small perforation of esoph- agus at site of operative injury Suture line intact
J G M 57	3 mos	40	Adeno- carci- noma	6-4-41 Abdominal exploration inoperable	None	Alive	
R M M 55	4 wks	30	Adeno- carci- noma	8-6-41 Abdominal exploration adherent to pancreas metastases to diaphragm	None	Alive	

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spond to medical treatment. While the clinical and pathological evidence of malignant degeneration of a pre-existing ulcer in these cases is more speculative than real, the course of events is certainly most suggestive.

The general examination of a patient suspected of harboring a cancer of the cardia rarely yields positive findings. Occasionally one may demonstrate an enlarged lymph node in the left supraclavicular fossa, the Virchow node. Unusual hardness of this node or fixation to surrounding tissues is an indication for biopsy to demonstrate metastatic involvement. Rarely can one palpate the tumor on abdominal examination. Metastatic liver involvement may or may not be demonstrated by palpation. It is important not to omit rectal examination to exclude metastases to the rectal shelf.

Every patient presenting the symptoms enumerated should be referred to a competent radiologist for roentgenographic visualization of the esophagus and stomach. In most instances, the presence of a tumor will be clearly demonstrated by the usual methods. The most common roentgenographic findings are obstruction of the lower esophagus, irregular filling defects at the cardia, rigidity of the lesser curvature on fluoroscopic observation and loss of the normal mucosal pattern. It may be extremely difficult to demonstrate any abnormality when the tumor is located on the posterior wall toward the incisure. Persistency on the part of the examiner with the aid of a heavier mixture of barium and the taking of multiple films in the lateral, oblique, recumbent, and standing positions will usually demonstrate the growth.

Every patient presenting the symptom of dysphagia, associated with positive findings in the x-ray films, should, in my opinion, be subjected to esophagoscopic examination. This is an important part of the complete work-up. The esophagoscopist accurately locates the upper level of the tumor with respect to the distance of the upper incisor teeth and thereby guides the surgeon in his operative approach. Histological examination of the biopsy specimen will indicate whether the tumor has originated from the stomach mucosa, or from esophagus. I have preferred esophagoscopy to gastroscopy because with the former more accurate visualization of the tumor may be obtained, and at the same time, a biopsy specimen may be secured. In the hands of a competent operator there is little difference in the risk of the two procedures.

Once the decision to attempt radical extirpation of carcinoma of the cardia is made a period of preparation for the ordeal is in order. In previous

publications I have elaborated on the details of this pre-operative preparation and will not discuss them at this time. Suffice it to say that this should include careful attention to oral hygiene, high caloric liquid diet, parenteral administration of vitamins, the administration of fluids by venoclysis, recently the use of intravenous amino acids both before and after operation, and a preoperative transfusion of whole blood. On the basis of our favorable experience with the preoperative administration of galliumbamide in colonic surgery as reported by Garlock and Seley, I have routinely administered this drug to patients with cancer of the cardia for 72 hours prior to operation. It is my impression that this drug has been a considerable factor in minimizing infection. The recent report by Seley and Colp concerning the bacteriological studies in cancer of the stomach is confirmatory evidence of this opinion.

The demonstration of adenocarcinoma in the biopsy specimen will immediately indicate to the surgeon the plan of surgical attack to be adopted. There seems to be general agreement at the present time that the operation of choice for cancer of the lower esophagus and cardiac end of the stomach is a left transthoracic, transdiaphragmatic resection with intrathoracic esophagogastronomy. Any other operative procedure which is limited to an abdominal approach falls far short of the ideal sought for in the radical surgical treatment of cancer anywhere, namely, free exposure and complete visualization of the field of operation. However, because the lymphatic spread of cancers of the cardia is most often in a peripheral direction *below the diaphragm*, it is important to determine operability without exposing the patient unnecessarily to the risks of transthoracic exploration. For this reason, I suggested some time ago that exploration be carried out through a small upper left rectus incision. Palpation will quickly indicate whether the tumor is resectable. Metastases to the liver or to the pancreatic lymph nodes and fixation of the growth to neighboring vital structures are contraindications to further surgery. Rarely abdominal exploration will indicate operability yet, when the chest is opened extensive mediastinal node involvement will be demonstrated. This, in my experience is so infrequent that it may be considered only as a remote possibility.

If the tumor seems resectable, the wound may be closed quickly with buried figure of eight steel wire sutures and skin clips. The patient is now turned on his right side and, following change in the operative setup the left thoracic cavity is entered through the eighth interspace. Those

interested in the details of the operative procedure are referred to previous publications on the subject. Briefly, the operation, considerably modified from the original Fischer and Sauerbruch procedures, includes division of the eighth, seventh, and sixth ribs close to the spine, mobilization of the distal esophagus, radial incision of the left leaf of the diaphragm, mobilization of the upper two-thirds of the stomach by dividing the left gastric artery and the left gastroepiploic vessels, resection of the tumor-bearing portion with a wide margin of normal tissue, block dissection of the associated lymph nodes with the primary tumor, the performance of a two layer silk suture anastomosis between the end of the esophagus and the anterior wall of the stomach, and the telescoping of the esophagus into the stomach in order to obviate tension on the suture line. Under water drainage of the pleural cavity by a tube inserted through a stab wound in the subjacent intercostal space completes the operation. I believe it is important that every patient receive a transfusion during the course of the operation. In every case, I have employed positive pressure ethylene or cyclopropane anesthesia after a basal dose of avertin. Intratracheal anesthesia may also be used, provided that the trauma of intubation is minimal.

Reference should be made to the advisability of staging the operation so as to diminish the likelihood of operative shock. Marshall, in his case report in 1938, divided the operation into two stages. At the first operation, through an abdominal approach, the blood supply of the upper part of the stomach was ablated and the mobilized portion was pushed up into the posterior mediastinum through the surgically enlarged esophageal hiatus. Approximately 2 weeks later, the second stage was performed and consisted of a left transthoracic resection with anastomosis. My objection to staging the operation in this manner is threefold. In the first place, during the first stage, it is impossible to demonstrate mediastinal node involvement, second, it is technically easier to free the upper end of the stomach by the transthoracic, transdiaphragmatic approach than from the abdominal side, and in addition, the entire field of operation is more clearly visualized, and third, operative shock has not been a factor in the causes of postoperative mortality. If bleeding is carefully controlled, if tissue trauma is reduced to a minimum and if the patient is transfused during the course of the operation, surprisingly little shock will be noted. The operating time for the one stage procedure has varied between 2 hours and 2 hours and 30 minutes. For the reasons stated, I prefer the one stage operation.

Experience has proved that the operation of resection of the upper stomach with intrathoracic esophagogastrostomy is physiologically sound and that solid healing takes place at the site of suture. Including a group of squamous cell cancers of the distal esophagus, I have carried out this operation in 16 cases and in not one instance has there been any evidence of dehiscence of the suture line or leakage. I, therefore, see no reason for employing any of the complicated procedures to protect the suture line such as were recently reported and which were based only upon observations made in the experimental laboratory.

Before the operation is undertaken, it is important to explain to the patient that he must not swallow for a period of 4 or 5 days. The processes of repair at the suture line will be hastened by the full co-operation of the patient in this respect. Fluids are administered by a continuous intravenous drip of 5 per cent glucose in normal saline.

The character of the material draining through the intercostal tube will indicate the progress of the intrathoracic situation. During the first 48 hours, the fluid is sanguineous. After this, it gradually assumes a lighter color and decreases in amount until the seventh or eighth day when the tube may be removed.

Small sips of water may be given on the fourth or fifth day. Increasing amounts of liquid are given until the twelfth or thirteenth day when custards, gelatins, cereals, etc., are permitted. The diet is rapidly increased thereafter. Solid food should not be given until the third week.

As with adenocarcinoma of the rest of the gastrointestinal tract, the results of radiation therapy have been extremely disappointing. Even the direct exposure of the tumor by the use of a special intragastric tube, as reported by Pack and others, has failed to show results sufficiently encouraging to warrant substituting this method of treatment for direct surgical attack. Unless obvious contraindications exist, I believe every patient with a cancer of the upper end of the stomach should be explored to determine operability. If this plan is followed, it is obvious that many more successful resections will be carried out.

RESULTS

During the past 4 years, I have explored 25 patients with adenocarcinoma of the cardiac end of the stomach. Nine were found operable, an operability percentage of 36. There was no operative mortality in the inoperable group. Nine patients were subjected to the radical operation. There were 4 postoperative deaths, an operative mortality of 44.4 per cent. Of the 5 survivors, 1 patient

died of retroperitoneal metastases 136 years after operation. The 4 remaining patients are alive and well (no evidence of recurrence) 18 months, 17 months, 8 months, and 7 months, respectively. The essential details of the entire series are tabulated in Table I.

SUMMARY AND CONCLUSIONS

Until recently cancer of the upper end of the stomach was generally considered beyond the scope of radical surgery and patients afflicted with the disease were placed in the hopeless group. With the development of the more accurate diagnostic procedures of roentgenography, esophagoscopy and gastroscopy an increasing number of patients in the early and perhaps curable stages of the disease is being referred for treatment. Whether such treatment should be by radiation methods or radical surgical extirpation, should, in my opinion, be a matter of little discussion. The results of radiation therapy of the most modern type have been universally disappointing and no cured case has, thus far, been recorded. On the other hand, with the modern improvements in surgical technique and recent advances in the field of anesthesia, surgery has much more to offer the patient harboring this disease. On the basis of the experience cited in this paper and in others already published, the patient with a resectable cancer of the upper end of the stomach has 60 per cent chance of surviving the operation and an 80 per cent probability of living more than 2 years. It remains for the medical profession to be alive to the possibility of the existence of a cancer

of the cardia in every patient who complains of persistent indigestion and difficulty in swallowing and to accept the operation of transthoracic resection with esophagogastronomy as a standard procedure, one which offers the patient the best chance of being cured of his disease.

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TRENDS IN CANCER RESEARCH

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ON behalf of the National Cancer Institute, I wish to acknowledge our indebtedness to the American College of Surgeons, first, for improving the standards of tumor clinics, which has been of great value to us in the effective distribution of radium loans and in the provision of free training for physicians in diagnosis and treatment¹, and second, for having kept alive the constructive interest of the medical profession and laity in the cancer problem.

Trends in any field of research change with time as new facts are discovered. Up to the end of the last century cancer research was confined to descriptive observations on cancer in man. Isolated reports of cancer in other mammals were ignored. Speculation was rampant as to causation. A remarkable exception was the keen observation of Percival Pott who, in 1775, recognized the possible relationship of coal soot and cancer of the scrotum in chimney sweeps. A century later, Virchow's hypothesis focused attention on the tissue cells, which were supposed to undergo malignant transformation as a result of "chronic irritation." Subsequent modifications of the cell theory attributed cancer to embryonic cell rests or to abnormal conditions during regeneration of injured tissues. With the recognition of the parasitic origin of certain diseases, the search for a specific infectious agent for cancer was let loose and to some extent has continued to this day. In retrospect it is clear that each one of these attempts to explain the causation of cancer had the weakness of oversimplifying the problem. At last, at the end of the nineteenth century, Claude Bernard's plea for controlled experimentation was applied to the cancer problem. As a result a large number of new facts have been discovered. The following discussion is restricted to mammalian neoplasms.

The first important conclusion reached from experimental work is the high specificity of malignant cells. Each one of the many types breeds true *in vivo* and *in vitro*. For instance, a mam-

mary carcinoma of the mouse transplanted into other susceptible mice reproduces itself in an unlimited series of generations. Furthermore, many types of malignant cells have been maintained in tissue culture for years without losing the ability to produce the specific tumors after being inoculated into the same strain of animals from which they were derived. The maintenance of such cultures over a long time requires an aseptic technique which is more strict than that used in surgery. The slightest infection as a rule causes the loss of cultures. It is difficult to bring these and other facts into harmony with the view that mammalian cancers are due to a specific infectious agent, especially since it has not been possible to isolate such agents from any tumors. Moreover, numerous attempts to produce curative serums without exception have failed. On the other hand it is established, both clinically and experimentally, that certain parasitic infections can predispose tissues to the development of cancer, but it should again be emphasized that these parasites do not play a specific rôle and are not detectable in the resulting neoplasms.

Basing their investigation on Pott's observation, Yamagiwa and Ichikawa in 1915 announced the production of skin cancer in rabbits by the long continued topical application of coal tar. This important discovery shifted the trend of cancer research into the field of chemistry. Through painstaking work a highly potent carcinogenic chemical, 3, 4-benzpyrene, was isolated from coal tar. At present the carcinogenic properties of about 250 synthetic chemicals have been recognized. Some of these, as 20-methylcholanthrene, have been extremely valuable for the experimental production in animals of almost every type of malignant tumor seen in man. Fractions of a milligram of this compound can produce malignant tumors at the site of injection or in distant organs.

The ease of chemical carcinogenesis has thrown much light on tumor histogenesis under controlled conditions (3, 6, 7). Morphologically recognizable tissue injury may occur but does not necessarily precede tumor formation. As exceptions, I mention induced as well as spontaneous pulmonary and mammary tumors. In fact, the term "chronic irritation," while still of value for cancer-control education, has outlived much of its scientific use-

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fulness in cancer research. The conversion of normal into malignant cells is apparently due to changes which are far too subtle to be analyzed exhaustively by the available histologic methods. Even the most refined cytologic technique at present fails to differentiate malignant cells from the cells of origin. After all, what we see through the microscope is only an infinitesimal part of what is present and going on in living cells. For this reason I have maintained for some years that carcinogenesis, as well as other fundamental cancer problems, should be attacked from the view point of cell physiology and biochemistry for we are dealing with a fundamental biological problem.

Work with chemical carcinogens has firmly established the fact that tumors appear only after a relatively long latent period, which depends on the type, dose, and method of administration of the chemical, the animal species and strain, and the sex (2). The great value of animals with a relatively short life span of 2 to 3 years, such as mice and rats, may well be due in part to the rapidity of aging which may be assumed also to speed up the cancer process. The physiological time factor is certainly important in human and animal carcinogenesis. Therefore, a better understanding of carcinogenesis will go hand in hand with a better understanding of the process of aging of which we know relatively little.

Another remarkable fact is the ease with which such a powerful chemical as methylcholanthrene can produce malignancies in a great variety of tissues, as the brain, skin, striated muscle, subcutaneous tissue, lung, etc. This lack of specificity with regard to the cell type involved deserves further study. It is, indeed, exceedingly important to explain the intricate mechanism of action of methylcholanthrene on any normal cell type which is known to be convertible into the malignant state. Work on this subject has been in progress for some time at the National Cancer Institute and elsewhere. We have found for instance, that prolonged exposure of cultures of normal subcutaneous mouse fibroblasts to high dilutions of methylcholanthrene causes apparently permanent changes in cell physiology comparable with those observed in cultures of sarcomas induced by methylcholanthrene in the subcutaneous tissue of mice of the same strain (4). Efforts are being continued to prove that carcinogenesis can take place *in vitro*. Positive results would indicate that carcinogenesis does not depend on favorable systemic conditions, but can be explained by a direct interaction between carcinogen and cell.

Recently some progress has been made in the study of the dietary factor in the production of induced tumors. These cells are highly organized biochemical units. Their normal function depends partly on a continuous supply of energy yielding chemicals and of other chemicals which are needed for the construction of cell proteins, lipids, and carbohydrates, or for the regulation of cell activity as enzymes and vitamins. Hence it is logical to consider the composition of the diet as a possible modifying factor in carcinogenesis. Some years ago, we (19, 20) showed that the growth rate of spontaneous mammary carcinomas in mice could be strikingly inhibited by diets deficient in certain essential amino acids. This inhibition of tumor growth was not accompanied by any evidence of general malnutrition. Recently other workers found that the development of hepatomas in rats induced by the azo dye butter yellow can be considerably delayed by certain diets (16). Work at our Institute (23) has also shown that the response of mice to skin painting with methylcholanthrene is strikingly influenced by the composition of the diet. If the diet contains an adequate amount of the amino acid, cystine, the mice develop acute leucemias with great regularity. On a low cystine diet however the development of leucemia is greatly retarded, and instead the mice exhibit extensive atherosclerotic lesions of the larger arteries.

Butter yellow and methylcholanthrene are toxic for young rats maintained on a diet low in cystine. The growth rate is strikingly inhibited and is accelerated as soon as cystine is added to the diet (3, 24). Dietary cystine may be regarded as a detoxicating agent for the two chemical carcinogens in question. Hepatoma formation by butter yellow is accompanied by severe liver injury and liver cirrhosis, which may or may not be a requisite for hepatoma formation (5). It is not easy therefore to differentiate the specific carcinogenic action from the nonspecific toxicity. Similar work on spontaneous tumors has also yielded results indicating dietary influence.

It has been suggested that abnormal diets may play a part in the causation of gastrointestinal tumors, an idea which at least has the merit of stimulating research. Roffo reported that rats which are maintained for a long time on a diet containing boiled fats develop gastric adenocarcinoma. Careful work at our Institute so far has

After Holt and Anderson, of the Institute, recently made the following observations upon C3H mice when groups of age were divided into groups. One group was fed relatively low protein-low cystine diet and the other relatively low protein-high cystine diet. At the end of 26 months all mice on the high cystine diet had developed spontaneous mammary tumors, whereas at the same time of the mice on the low cystine diet had mammary tumors.

not confirmed this claim. On the other hand, we have succeeded in producing for the first time gastrointestinal carcinoma in mice by means of methylcholanthrene (15). The forestomach of the mouse is lined by squamous epithelium and the rest of the organ by glandular mucosa. Spontaneous gastrointestinal tumors have never been observed in the mice used. At first the carcinogen was given continuously to the mice as a dilute emulsion in the drinking water. After many months there occurred squamous cell carcinomas in the forestomach, whereas the glandular portion was normal. Some of the animals also developed typical carcinoma of the small intestine (13). This curious susceptibility to malignant change of gastric squamous epithelium and the apparent lack of susceptibility of the gastric glandular mucosa must be explained. Can it be due to the inability of the carcinogen to penetrate into the gastric mucosa? To test this, a small volume of a dispersion of methylcholanthrene was injected into the glandular mucosa of mice of the same strains. Up to the present five typical adenocarcinomas have thus been produced at the site of injection. One of these tumors has been successfully transplanted subcutaneously into other mice. The transplants grow rapidly, and the tumors have retained their histological structure in two generations. To me the most interesting point is the probability that the layer of gastric mucus functions as a protective barrier when the carcinogen is given orally. If this be true, it follows that the production of gastric adenocarcinoma by carcinogenic dietary components, if such exist, may be conditioned by a break in the mucus barrier under pathological conditions.

The discovery of the artificial chemical carcinogens is a milestone in cancer research as it has made possible the experimental production of tumors under controlled conditions. Nevertheless, the great unsolved problem still is the causation of so called spontaneous neoplasms. The case with which the artificial agents produce tumors strengthens the belief that the naturally occurring tumors are caused by chemicals formed within the body. In fact, it is firmly established that very large doses of female sex hormones acting over a long time can induce malignant tumors of the breast and uterus in mice and rats. Furthermore, experiments with different inbred strains of mice have revealed a unique influence of the mother's milk on the development of mammary cancer in the offspring (1). Foster nursing of newly born female mice from a strain with a normally high tumor incidence by a mother of a low tumor strain strikingly decreases the tumor incidence in the foster nursed animals. On the other hand, foster nursing of young females from a strain with a normally low tumor incidence by a mother of a high tumor strain greatly increases the tumor incidence in the fostered mice. Work on the nature of the agents responsible for these effects is in progress at our Institute, as is also the question as to whether or not the findings apply to human mammary carcinoma.

Mention may now be made of recent claims of the carcinogenic action of cell free extracts of tissues and of urine from cancer patients. This work is based on the assumption that as a consequence of abnormal metabolism endogenic substances exert a carcinogenic action. The first report in this field was made by the Russian scientist Shabad (12). He extracted grossly normal livers of individuals dead from cancer of the stomach, lung, and other organs, with benzene, since benzene is a good solvent for many carcinogenic hydrocarbons, sterols, and bile acids. After evaporation of the benzene extract the residue was injected subcutaneously into mice. This caused local tissue destruction and killed some of the animals. Malignant tumors were observed after 8 months or longer, both at the injection site and in distant organs. Few tumors also occurred in nontreated control mice. Similar results have been reported by British and American investigators. Taken as a whole, these findings should be accepted with considerable caution. While there is no doubt that malignant tumors were observed, it is premature to accept this evidence as conclusive proof for the existence of endogenic carcinogenic chemicals in cancer patients. Most of the tumors appeared after a very long latent period and in a relatively low percentage of injected animals. Sesame oil was used by some as a solvent, an oil which is known to cause subcutaneous sarcomas occasionally. Other workers used a rather drastic chemical method for the preparation of the test material, which leaves some doubt as to whether the carcinogenic material was preformed. Final proof must wait, therefore, until the agents are isolated in chemically pure form and until it is shown that the sufficient concentration and can act over a sufficient time to induce tumors. This line of investigation serves as an illustration of the great effort and time required to establish fundamental facts in cancer research.

Brief mention should now be made of work designed to explain the difference in behavior of malignant and normal cells. Here again the biochemical approach seems to be advantageous.

since it is reasonable to suppose that the difference in behavior may be due to differences in biochemical organization. One of the chief difficulties is the availability of a suitable control tissue for a given tumor (17). We have recently used liver of the rat for comparison with a rat hepatoma. The regenerating liver serves as a comparison of a proliferating normal tissue with the proliferating liver tumor. The results so far obtained indicate that the tumor is characterized by a high anaerobic and aerobic lactic acid production and a respiratory quotient below unity² by a very low content in riboflavin (o) and coenzyme (12) by a great reduction in glycogen (6) with an apparent unchanged amylase activity and, most striking, by a reduction in the catalase activity to one one thousandth of that of the normal control tissues (9). The activity of some other enzymes seems to be unchanged. In short it appears that some of the important enzymatic activities of the tumor show marked decreases, which may perhaps account for the specific tumor biology. It is evident that whatever differences have been found are of a quantitative not a qualitative nature.

Another line of inquiry which in the past has been ignored deals with the systemic influence of cancerous growth as evidenced by cancer cachexia. Here again biochemistry may be helpful. I have just referred to the great diminution of catalase in the rat hepatoma. Work at the Institute has shown that the catalase activity of the morphologically normal liver of rats carrying large subcutaneous hepatoma transplant is reduced to less than one-tenth of that of the liver catalase of a normal rat. This effect is easily reversible, because after extirpation of the tumor the liver catalase returns to normal within 48 hours (8). Since catalase functions in the chain of oxidative reactions in tissue metabolism, it is rather interesting to find very great reduction in catalase activity in the hepatic tumor and lesser decrease in the apparently normal liver of the tumor bearing animal. Unpublished data indicate that this decrease in liver catalase occurs also with other rapidly growing malignant tumors. Further studies may lead to information of use for correcting the pathological cancer metabolism.

As to research on diagnosis and treatment, I must refer to my Barnard lecture of a year ago (18).

CONCLUSION

In conclusion I have tried to formulate some phases of cancer research and to report in a general way on the progress which is being made. Emphasis has been placed on the study of carcinogenesis, since hope of preventing cancer not only the so called occupational but also the spontaneous neoplasms, must be based on such studies. I have also stressed the importance of work aimed at a better understanding of the behavior of cancer cells in comparison with the normal cells of origin. Great difficulties are met in the study of these problems in human beings. The limitations of purely morphologic studies were mentioned and the value of physiologic and biochemical approach was pointed out. The outlook is good for further progress from combined laboratory and clinical research. Under present world conditions, the main responsibility for such studies for years will rest on American investigators.

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²Work carried out in the Department of Biochemistry, Cornell Medical School.

³The first indication of systematic biochemical action of the growth of two malignant tumors was reported some years ago (19). It was found that the neoplastic cells of these two tumors of the same histological type showed progressive decrease with increasing tumor growth.

THE IMPORTANCE OF A COMPLETE DIAGNOSIS TO A SUCCESSFUL TREATMENT OF STRABISMUS

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AS in all branches of medicine, a complete diagnosis must be made before an intelligent course of treatment can be instituted with any hope of a successful termination. The day is past when convergent strabismus can be considered always due to hypermetropia and a divergent strabismus due to myopia or to a so called anomalous position of rest.

A divergent strabismus is not uncommon in a high hyperope, nor is a convergent strabismus uncommon in a myope of even a low degree.

A vertical strabismus may be seen occasionally without an elevator or depressor being involved—in other words, due to an anomaly of sursumvergence—but in my experience this is most unusual.

The usual observation is that a large percentage of cases of lateral strabismus have a vertical element, which is a varying factor in the development of the lateral squint.

A certain number of cases of convergent strabismus of the convergence excess type are corrected completely by a full correction of the hypermetropia, augmented if necessary by orthoptic training, but many cases of low or high degree of hypermetropia are but little, if any, affected by a correction of the ametropia. Many patients are seen with a hypermetropia of low degree and a strabismus of 60 to 80 prism diopters, or again, with a hypermetropia from 2 diopters up, in which a full correction of the ametropia has really no appreciable effect on the strabismus. Discussion of the various theories has continued many years but our patients come and go while we are trying to find one solution to the whole problem as to diagnosis and treatment, be it operative or nonoperative.

I must quote again from McReynolds, of Dallas, who said in my hearing, "Every ophthalmologist who has ever had insomnia has devised a new operation or modification of a former procedure for the surgical correction of convergent strabismus, and, furthermore, every ophthalmologist at some time had insomnia."

I believe that the unsatisfactory results from operations and the unsuccessful search for one procedure that will be generally adopted for the cor-

rection of squints are due to the failure of the operator properly to determine and evaluate the several factors that may enter into the production of any given squint, and that nonsurgical or surgical treatment will vary as the exact type of strabismus varies. This statement includes convergent, divergent, and vertical squints and any combination of these.

Stated briefly, the various factors entering in the production of squints are:

1. An anomaly of one or more of the individual muscles. This may be from a faulty structure of the muscles, from a faulty insertion of the muscle, or from a faulty innervation. Each of these may have an added anomaly due to secondary contraction, secondary deviation, or to a primarily overacting muscle, as is occasionally seen in the large hypertrophic muscles.

Hence any squint should be studied first as to the possibility of an anomaly of any of the extraocular muscles.

2. The disjunctive acts of convergence, divergence, and sursumvergence.

Given a case of convergent strabismus in which individual muscle involvement has been eliminated, is the deviation greater for distance than for near? If greater for distance, it proves quite conclusively a primary divergence insufficiency, but if it is greater for near, it is primarily a convergence excess. If it is determined to be a convergence excess, is it due to hypermetropia, myopia, to a vertical imbalance, or may it be due to nervous irritation?

If a divergent strabismus is present and again the individual lateral muscles are normal, is the deviation greater for distance than for near? If greater for distance, it is a primary divergence excess, but if greater for near, it is primarily a convergence insufficiency. In either case, is the condition caused or modified by the kind or amount of ametropia or may an associated vertical imbalance be a main or contributing factor? In a conversation with F. W. Marlow, I stated that I believed that over 70 per cent of cases of divergence excess had a vertical anomaly. He had statistics to prove that nearer 85 per cent were so complicated. My experience is that most cases of

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anomalies of convergence are primarily due to a vertical anomaly of another variety

TESTS

Examination should include tests to determine deviation for distance and for near. At some time in the examination, these tests should be made with and without any ametropia being corrected. The effect of complete cycloplegia should be noted also the correction of any vertical anomaly. The deviation should be measured in the 6 cardinal fields and, if a strabismus, the fixing eye in each field should be determined. The power of convergence should be studied and it should be determined whether this is affected by correction of an ametropia or vertical imbalance. The presence and degree of binocular fixation or suppression should be determined. The history of heredity, illness, birth, or other injuries should be investigated. Not the least of the contributing factors is the nervous mechanism of the patient.

Squints may be caused by chorea, hysteria, and other neurological conditions. If it is possible for these to be the sole cause, how probable it is that they may be a contributing factor when hypermetropia, myopia, astigmatism, or any of the afore mentioned causes are present. Very frequently the convergent strabismus is worse when the patient is ill, overtired, or excited or a divergent strabismus is noticed only when a child is "day dreaming."

When one has clearly in mind the things to be observed the method of testing may be quite optional. It is unnecessary to state that my preference is for the cover test with the amounts of deviation measured by prisms. It is purely an objective test, can be used in any patient who has vision enough or is old enough to fix any chosen object, and it depends solely on the examiner's understanding of muscle anomalies and upon his powers of observation.

TREATMENT

After consideration of a patient with these different factors in mind and with some estimation

of their relative importance in producing the given squint treatment can be intelligently begun.

If for example, glasses definitely lessen the strabismus almost at once one is encouraged to expect a continued improvement, but if they have little or no effect within a month, then another factor is present which has not been given its due importance. This may be any one or more of the causes stated previously. Orthoptic training is in some cases a most helpful adjunct, but when orthoptic training is prescribed to a majority of patients with heterotropia, it is done through ignorance or dishonesty and may do much harm. Orthoptic training has a larger field in heterophoria, but even here the field of usefulness is definitely limited.

As soon as the ophthalmologist has determined that the results from different forms of nonoperative treatment are not giving the desired results or knows from experience that any form of nonoperative treatment will be a disappointment and expense then surgery should be considered and the sooner the better.

SUMMARY

1. An examination should be made as soon as a muscle anomaly is observed or suspected.
2. If it is impossible to make an exact differential diagnosis at once, the patient should be re-examined at intervals until such diagnosis is made.
3. The effect of various methods of treatment should be observed, by using those that will most probably prove the points in question.
4. These methods include consideration of the effects of cycloplegia, correction of an existing ametropia, correction of a vertical imbalance, and the results of the fusional tests and orthoptic training.
5. A complex either of inferiority or of defense commonly develops in cases of strabismus and often at a very early age.
6. When a patient so studied fails to respond satisfactorily to any probable nonoperative treatment, surgery should be considered and before school age unless there is a definite contraindication.

SURGICAL MANAGEMENT OF HETEROPHORIA

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HETEROPHORIA may be defined as a break in the amplitude of fusion, or the decompensation of muscle balance is maintained by fusion and the neuromuscular mechanism. Having diagnosed the presence and type of a phoria, the question of treatment presents itself. The diagnosis and the medical treatment with glasses, prisms, and orthoptic exercises, is not the function of this assignment. These most important points have been or will be discussed in the symposium. But it is necessary to emphasize that the decision to operate rests squarely on them. The analysis of the individual case is the prime requisite of surgical judgment. Success or failure in ocular muscle surgery particularly, depends entirely on the accuracy of our presurgical study and conclusions.

Lancaster said "the two things for which we strive in operating are, first, a position of orthophoria since, other things being equal, the nearer the eyes to a position of orthophoria, the less the task of the neuromuscular mechanism in maintaining binocular vision, second, an effective range of fusion, this being, if possible, even more important than the former. A neuromuscular mechanism, for example, may be made to produce an orthophoria by so shifting the position of the eyes in the orbits that approximately the same working of the controls will now result in orthophoria because the eyes start from a position nearer the ideal one. The idea that the purpose of operating on the ocular muscle is to weaken or to strengthen some muscle which is too strong or too weak is unsound physiologically."

Having concluded that operation is necessary, a conclusion often arrived at only after repeated interval observations, two questions arise (1) when to operate, (2) what to do and how much. The first question can be simply answered. I think that one should operate when a phoria produces symptoms that can be relieved in no other way, provided that there is some degree of fusion power available and capable of being increased in its amplitude. This is particularly applicable to hyperphoria when it may happen that the patient has not suppression of the false image but it does not cause trouble because it is so far

from the true image. The more closely the false image is approached to the true one without fusion the more annoying it becomes. Such patients are not grateful.

The age of the patient, I believe, makes little difference although it seems wise to overcorrect an exophoria and undercorrect an esophoria in the very young (under 8 years). It has been my experience that adduction decreases and abduction increases with age. Phorias, particularly of high degree, may easily develop into tropias without the child complaining. It is easier to learn suppression when very young and when the fusion impulse is not as strong as it is later. Older children and particularly adults, complain of diplopia, occasionally for a long time, when fusion decompensation occurs. Such decompensation may occur as the result of age, illness, or fatigue. The learning of suppression takes much longer in these cases and for that reason the adult himself seeks relief from the annoying diplopia.

The second problem, what to do surgically, and how much, is more difficult of solution. I shall leave to our distinguished South American confrère, Dr. Alvaro, the task of describing the modern surgical techniques employed in squint, since these maneuvers are the same for the phorias as for the tropias, with few exceptions. The choice of the type of operation is that with which the surgeon is thoroughly experienced and skilled. Since the object of surgery in the phorias is to facilitate fusion, it is not necessary to do as much, I think, as in the tropias. In other words, it seems better to do too little than too much. Although with modern materials and techniques the chances of sutures slipping and making matters worse are not nearly as great as hitherto, such cases do occur and must be guarded against. For this reason it would seem better to restrict the operations to recession or at least controlled or partial tenotomy for lengthening, and tucking or the O'Connor cinch operations for shortening.

The choice of an anesthetic is that of individual opinion. Many prefer local anesthesia, injecting the anesthetic well back into the belly of the muscle in the orbit in order to obviate, if possible, the annoying edema of the muscle at its attachment. A general anesthetic, particularly when given through an intratracheal tube thereby freeing the field of cumbersome masks, appears to be

ideal for all ages, provided of course that there are no contraindications.

Whatever operation is done must be done meticulously. The various steps of the operation from the conjunctival incision to its final closure must be methodical, painstaking and surgically precise. Tenon's capsule must be preserved as far as possible; the muscle and tendon bruised as little as is necessary and the wound closed completely if one wishes to avoid postoperative trouble.

Since we are dealing with living tissue and not mathematic figures the problem of just how much to do is indeed a thorny one. Many times it appears to be solved only by intuition based on many years of bitter experience. The causes of failure are many and discouraging but if a proper analysis of the case has been made, particularly the investigation of hyperphoria, the percentage of failures will necessarily decrease. Too often is the presence of hyperphoria missed. It is much more common than thought, as can be seen by the analysis of 1,955 cases of ocular motor anomalies by White and Brown, who found that 36.6 per cent had an accompanying vertical anomaly. They concluded

"In uncomplicated convergence excess with either lower or higher degree of hypermetropia, double recession will give most satisfactory result. However, when vertical imbalance is present, the same amount of recession for an equal amount of lateral squint may result occasionally in undercorrection but more frequently in overcorrection, about as much as the original squint. This result may be delayed or it may develop immediately after operation.

In uncomplicated divergence excess with normal convergences near-point, conservative recession of one or both external rectus muscles gives good result. In the presence of vertical imbalance, there may be an undercorrection, but much more probably marked overcorrection.

In convergence insufficiency with secondary divergence excess, or when the divergence excess is primary and can judge the operative results accurately when there is no vertical imbalance. But in the presence of complicating hypermetropia, the same amount of recession or resection may result in "definite overcorrection, but much more probably there will be an undercorrection of the lateral deviation.

"These failures will become less frequent if the vertical imbalance can be corrected before the lateral imbalance.

Certain general rules have been laid down by the experience of others in an effort to determine what to do in average cases. A table of such rules can be found in Spaeth's *Principles and Practice of Ophthalmic Surgery* because it will be found useful as a starting point it is worthy of emphasis.

The rules for hyperphoria must be briefly and vaguely stated. It is agreed that surgery should be directed to the hypophoric eye although it may be necessary to divide this between the two because of a great degree of hyperphoria. It

TABLE I—RULES FOR DECIDING ON SURGICAL PROCEDURES FOR THE PHORIAS (SPAETH)

I. Phoria	Individual type	Surgery
Esophoria	Accommodative esophoria in both eyes, convergence insufficiency not such, proportionate to degree of myopia	Tucking or resection of one or both internal recti
	Convergence insufficiency esophoria for near and distance, measurement of prism indicates there is deviation defect to be in the distance but not in the near deviation ratio	Tucking or resection of one or both internal recti. May need increase of one external rectus as well
	Divergence excess, esophoria for both near and distance. Undercorrection	Recession of both internal recti
Exophoria	Convergence excess. Deviation greater than value	Recession of both internal recti
	Divergence insufficiency	Tucking or resection of one or both internal recti

should be recalled that double hyperphoria is usually not a surgical condition but is a pure innervational defect. Operation, however, should be considered at times when the double hyperphoria is decidedly unequal. One should do either a recession of the overacting muscle or tucking or the pinch operation on the underacting muscle in the hypophoric eye combined with operation on the hyperphoric eye as may be indicated. It is, indeed, wise to do a little at a time in the correction of hyperphoria, rather than too much at one sitting. Sometimes one should allow an interval of time for example 3 to 5 months, between operations on the vertical muscles. During this interval orthoptic exercises may be used with advantage. The surgical correction of hyperphoria is fraught with difficulties and errors of judgment and constitutes the most difficult problem in ophthalmic surgery.

The same can be said for cyclophoria. Indeed, so easily can this condition be made worse from the patient's viewpoint, that only the most expert muscle surgeon should tackle this problem.

One can conclude, therefore, by reiterating the statement that the surgical management of heterophoria depends fundamentally on the accurate diagnosis and skillful analysis of its factors, and that each case is a law unto itself. The diagnosis and not the actual performance is what counts.

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TUMORS OF THE SALIVARY GLANDS, BENIGN AND LOCALLY MALIGNANT

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SALIVARY gland tumors are probably the most debatable of all tumors and have been for many years. There are those which are definitely benign and those which are definitely malignant, but the largest group and most controversial is the mixed tumor which is benign in that it rarely metastasizes but malignant in that local recurrence is a predominating characteristic.

Parotid cysts may be congenital, but they are usually secondary to chronic infection or duct obstruction. They are often without symptoms but more often marked by the presence of swelling over the gland with pain and tenderness which may disappear with the emptying of the ducts. After a time the obstruction becomes more complete with infection complicating the picture. When suppuration occurs, external drainage may be resorted to. Following drainage complicating salivary fistulas may result, therefore, every effort should be made to avoid operative interference. In several instances, we have seen these troublesome cystic glands cured by x-ray therapy. If sufficient radiation is given, the gland atrophies, becoming functionless, and the cysts give no further trouble. This is a great improvement over former attempts to dissect out the cysts.

Mikulicz's disease, because of the peculiarity of the condition and the unexplained etiology, cannot be ignored in the discussion of tumors of the salivary glands. While enlargement of the salivary, particularly the parotid, and lacrimal glands may be associated with leucemia, tuberculosis, lymphosarcoma, and toxic conditions, and has been given the name of Mikulicz's syndrome, the condition described by Mikulicz in 1888 was a definite condition without constitutional symptoms. The important part of the pathological anatomy of the disease is an extensive deposit of small round cells which seem to compress or displace the glandular parenchyma. These cells appear to be either an infiltration of leucocytes or multiplying lymphoid tissue ordinarily found in

the gland. The gland structure may be compressed or infiltrated with an excess of fibrous tissue as well. While the prognosis in these cases is difficult because of their rarity and the absence of final reports upon cases found in the literature, we think we can safely say that they are not serious and treatment is unnecessary. A case we observed exhibited no symptoms and little change in the condition over a 5 year period although the tumor of the lacrimal glands have had to be removed because of pressure upon the eyeball. Radiation should, and apparently does, have a beneficial effect in preventing the progress of the disease.

Adenolymphoma (onkocytoma) of the parotid gland is one of the rarest of tumors. It may not be directly in the salivary glands but often adjacent to them. It is composed of a lymphadenoid stroma with germinal centers with an epithelial structure in the form of tubular glands, cysts, and papillae (papillary cystadenolymphoma or papillary cystadenoma lymphomatosum). They occur in older people, are benign, encapsulated, and grow slowly. They are not usually intimately connected with the gland and may be easily removed without damage to the facial nerve or danger of recurrence.

Adenoma of the salivary gland is again one of the controversial tumors, and Warren (8) says, "Adenomas readily recognized as such are extremely rare in the salivary gland." If they do occur, it is in the parotid gland. They are always encapsulated and may be cystic or solid. The differential diagnosis between the adenoma and mixed tumor is hardly possible before operation.

Mixed tumors comprise the great majority of all tumors of the salivary glands and have been of particular interest to the profession for many years. The literature is fairly rich in discussions of this particular neoplasm. Because of the large size they may attain, years ago surgical attempts were made to remove them. I S Cutter wrote an interesting account of a controversy between the medical departments of the University of Pennsylvania and Jefferson Medical College as to priority in removal of the parotid gland. We quote

"In 1832, Dr William Gibson, professor of surgery in the University of Pennsylvania, in a lecture delivered late in the year, denied that the parotid gland had ever been extir-

TABLE I.—DISTRIBUTION OF 65 SALIVARY TUMORS

	Parotid gland		Submaxillary gland		Palate		Gum		Lacrimal	
	No.	Per cent	No.	Per cent	No.	Per cent	No.	Per cent	No.	Per cent
58 Primary salivary tumors	45	77.4	11	16.9	3	4.6				
43 Mixed tumors	37				6					
Malignant tumors		36.4								
Mortality rate	25 per cent		25 per cent							

pared. The founder of Jefferson, Dr. George McClellan, had already reported several cases of extirpation of the parotid and this surgical triumph had been set up as one of the household gods of the Jefferson student body. The letter to Professor Pattison was dated January 8, 1833, and concludes:

We, the students of Jefferson Medical College, feeling the honor of our Professor (McClellan) involved, and the credit of our Institution concerned, in the fact being fully established, could feel obliged to you, if you could enter into discussion of the question, *Was the Parotid Gland ever been extirpated?*

John Bell (in his *Autobiography*) said: "The cutting out completely of the parotid gland is a thing quite impossible, since the greater of all the arteries, viz., the temporal and the maxillary, lie absolutely imbedded in the gland."

John Bell later revised his original doctrine in his treatise on surgery stating that he had often extirpated the diseased parotid and his brother Sir Charles Bell says that he had assisted John in the extirpation of the gland.

McClellan performed the operation successfully a number of times. Agnew recorded that Warren removed the parotid gland first in 1798 and McClellan's first case was in 1805.

The long interest in the mixed tumors has not been because of a high mortality from disease but from the fact that the embryology and pathology are without a satisfactory explanation and also because the treatment of them is still unsolved in spite of persistent effort on the part of the pathologist, the surgeon and recently the roentgenologist.

The mixed tumors are defined by Harvey Dawson and Innes as adenomas of the serous and seromucous salivary or lacrimal glands, of undifferentiated and gland-lobular types, which are very prone to a species of mucoid autolytic self-destructive transformation of their component tissues and are seldom truly malignant.

Sill, Swinton and Warren say

The frequent tendency of epithelial cells to take on spindle form has also been used to explain the apparent mesenchymal structure of certain of the elements of the so called mixed tumors. There are however certain objections to the consideration of the mixed tumors as adenomas with peculiar stromal changes. Adenomas readily recognized as such are extremely rare in the salivary gland. Moreover this particular type of change in the stroma is

almost unknown in adenomas developing elsewhere. It seems peculiar that in this group of glands alone peculiar stromal changes should develop in the adenomas which arise from them. In the very few instances of the true adenomas which have been reported there is no suggestion of the structure seen in the mixed tumor.

The concept of true mixed tumor developing from embryonic tissue is far more appealing. Distinctly in favor of this is the not infrequent occurrence of mixed tumors in diverse localities, such as the hard palate, the buccal fossa, the soft palate, the cheek, or the gum.

These tumors were at first thought to be purely epithelial in origin. Virchow thought that the cartilage was formed by pieces of metaplasia from connective tissue while Cohnheim considered it to be a remnant of the branchial arches which became displaced during fetal life. The endothelial theory set forth by Wartman has been abandoned and the epithelial generally accepted, particularly since the investigations of Kenyon and Fry.

The figures given by McFarland for the relative occurrence of mixed tumors are parotid, 93.6 per cent; submaxillary, 6.2 per cent, and sublingual, 0.3 per cent. They probably represent an unselected distribution of tumor occurrence for the glands concerned. Harvey and his co-workers studied 316 mixed tumors, and the locality was given or evident in 275 of these cases: parotid gland, 230; submaxillary 21; sublingual, 2; lip, 9; palate, 6; nose, 1 and lacrimal, 6.

An analytical report of the cases of salivary gland tumor treated in the John Sealy Hospital and a study and comparative review of these tumors and others which have found their way into the Surgical Pathology Museum of the Medical Department of the University of Texas is summarized in Table I.

Of the 58 tumors arising primarily in the salivary tissues, 43 or 74 per cent were mixed tumors, and 15 or 26 per cent were carcinomatous, as shown in Table II. The distribution of these tumors according to location is given in Table I. Forty five tumors were in the parotid gland alone and of these 13 were malignant.

Symptomatically in the mixed tumors, pain or tenderness was noted in an occasional case. These

SINGLETON TUMORS OF THE SALIVARY GLANDS

TABLE II—COMPARISON STATISTICS

No of tumors	Singleton and Duren 58	Swinton and Warren 67	Stein and Geschickter 241 (parotid)	McFarland 300	Houck 40	Patey 55	Total No 766	Revised averages	
								yr	Per cent
Per cent malignancy in salivary tumors	25 8	12 5	17 4		40 5		412		20 4
Age at onset in years	31 5	33 3					122	32 4	
Mixed Malignant	52 3	56 2					122	54 2	
Preoperative duration in years	5 4	10 7	8 4				363	7 8	
Mixed Malignant	1 24	3 6					363	3 5	
Recurrence in mixed tumors including those recurrent when first seen—per cent	33 3	17 6		23 2	23 6		477		23 8
Recurrence in mixed tumors operated upon at John Sealy Hos pital	8 7% (J S H.)	4 3% (Labr, Clinlc)	12 8% (J S H.)				363		8 6

however, were usually in the cases of the recurrent or very large tumors. The malignant tumors commonly caused symptoms. More than one-half of the present 15 were associated with tenderness, pain, or facial paralysis. The pain was occasionally radiating. Fixation to surrounding tissues was commonly met with.

The average age at onset for all the primary tumors was 38 0 years. Of these, the mixed tumors averaged 31 5 years, and the malignant tumors, 52 3 years. The preoperative duration of the mixed tumors averaged 5 4 years, whereas the malignant tumors averaged 1 24 years. The sharp clinical differences comparable to the two histological groups is to be noted.

The recurrence rate of the 58 salivary tumors is divided into 2 groups. That rate which recurred after excision of the tumor both elsewhere and at John Sealy Hospital and that rate recurring in the cases of patients operated on at John Sealy Hospital only. The recurrence rate should be considered in this manner because many of the cases were recurrent when first seen at this hospital. These data are available in 45 cases. Of these, 34 were mixed tumors, 10 or 33 per cent recurred. Of these mixed tumors, 2 or 8 7 per cent recurred. One of the two recurrences among the mixed tumors occurred in an elderly woman. It was widely excised, but recurred in 6 months and after 1 year had reached large proportions. It was again widely excised. The case was followed for 1 year, at which time there had been no recurrence. This tumor showed an increased cellularity in the recurrent tumor. This, considered with the marked infiltrative character noted at operation, classifies this tumor as one of the most malignant of the mixed tumors.

There is considerable controversy over the rate of recurrence in relation to the size of these tumors. The cases on which sufficient data were available were computed with this in mind. McFarland, dividing his series into tumors up to a walnut in size and a walnut or larger in size, stated that 32 per cent of the former and 16 per cent of the latter recurred. Houck, however, noted 17 and 31 per cent recurrence rates, respectively. In our series, 13 3 per cent of the smaller and 40 per cent of the larger tumors recurred. These and Houck's findings are in direct variance with those of McFarland.

One explanation for the low recurrence rate, 8 per cent, of mixed tumors of patients operated upon by us at John Sealy Hospital was the practice of wide excision. This is reflected in the high rate of postoperative complications, that is, facial paralysis. Ten cases among the mixed tumors were complicated by permanent facial paralysis. Of these, 8 were total. Facial paralysis occurred in all but 2 of the carcinomatous parotid tumors operated on. Salivary fistulas rarely occurred. Two of the present series of cases were so complicated.

TREATMENT

The diagnosis of the mixed tumors of the salivary glands is usually possible by physical examination and a history of a long duration of the tumor. A mixed tumor may be found in various parts of the orofacial region. Occasionally they are found in the lip, palate, supramaxillary border, nose, bronchi, and lacrimal gland. When the tumors are found in these locations, the diagnoses may be suspected, but usually such is not the case until microscopic study reveals the identity of the tumors.

Two years ago we stated in a discussion of these tumors of the parotid gland (6)

Though the surgical treatment of tumors in various parts of the body has been standardized, that pertaining to the parotid salivary gland tumors is still in confusion, with wide variations in the opinion of the profession as to the plan to follow. Recurrences are frequent and therefore malignancy cannot be denied, but because of the infrequency of distant metastasis and the anatomic difficulty of extensive surgery without facial nerve injury incomplete or local operations are the rule. Investigation will reveal that the early experience of the surgeon will show strenuous effort to preserve the nerve but with more experience and increasing number of recurrences, more radical procedure is preferred with less regard for the nerve. Such has been our experience in dealing with the parotid tumors.

We also advocated radical surgery for carcinoma of the parotid gland, stating

Because of the uncertainty of prognosis the frankly malignant tumors are usually treated conservatively to save the facial nerve. Therefore, believe that conservative surgery is responsible for the high percentage of the recurrences, both in the mixed and malignant tumors. For some years we have felt that we are justified in removing large anastomata of the parotid gland and even all the gland in those cases where we are convinced that sacrificing the facial nerve was necessary for cure (6)

To justify radical removal of mixed tumors because of their possible transformation into carcinoma or sarcoma is questioned by good authorities. A few cases have been reported in which such a transformation has occurred, but they are rare. In 2 of our cases this seemed undeniable, but investigation of case histories does not justify this as a reason for radical surgery. One of the most incurable malignant tumors we have found is carcinoma of the parotid gland. Even with the most radical surgery early in the course of its growth, only a very few cures are on record. We have not seen one patient who has lived 5 years after treatment. This includes 15 definitely proved carcinomas of the parotid gland which we have operated upon in a radical way. Three of these are still free of recurrence, but a 5 year period has not yet elapsed in any one of these. McFarland reported 14 cases of carcinoma of the parotid gland, 1 of questionable diagnosis, and only 3 patients were alive 5 years and these had multiple operations for recurrence.

In the case of mixed tumors of the parotid, McFarland argues against removal when they are small, claiming that the recurrences are more like

ly in the small tumors. This is not the experience of others, including ourselves.

It requires tremendous restraint on the part of the surgeon to allow an ever prominent parotid tumor to be turned away without removal. In no other large group of tumors is the attitude of conservatism considered, but the all important complication facial nerve palsy which must follow radical surgery in this region is responsible for unsatisfactory results after their treatment. Unless it becomes large the tumor is preferable to a facial palsy. Many plastic procedures are used to counteract this distressing complication, some of which are satisfactory to a marked degree, but they are far short of completely correcting the deformity. The result appears unsatisfactory at first, but, unfortunately due to atrophy of anastomoses the deformity becomes more marked with the passage of time after most plastic procedures.

At the present time we have under observation a nurse who has a parotid tumor deep in the parotid gland directly in the path of the facial nerve. The tumor is not growing rapidly and, since a facial palsy would put an end to her profession as a nurse upon which she depends for her livelihood, I cannot to this time make up my mind to disturb it. McFarland's persistent and careful clinical study of a very large series of parotid tumors resulting in the conclusion that conservatism should be emphasized in their treatment, cannot be entirely disregarded. We could emphasize that every effort should be made to save the facial nerve, at least in the initial attempt at removal. A planned sacrifice of the facial nerve is justifiable in cases of recurrence and in carcinoma. Plastic repair is of great importance but does not prevent an objectionable deformity of the face.

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THE SULFONAMIDE DRUGS IN THE TREATMENT OF ACUTE SUPPURATIONS IN THE MIDDLE EAR AND MASTOID

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THE sulfonamide drugs met with prompt and enthusiastic acceptance in the field of otolaryngology where there remained many unsolved problems of coccal infections. The acceptance of these preparations was characterized at first by overenthusiasm and favorable prejudice. Although they have found a permanent place as some of the most valuable therapeutic agents in the otologists' armamentarium, they must not at once supplant other forms of treatment of proved worth.

One of the most controversial subjects referable to the use of these preparations is that pertaining to their efficacy in the treatment of acute suppurative otitis media and mastoiditis. Most otologists are willing to admit that since the use of sulfanilamide and sulfathiazole the incidence of surgical mastoiditis, the complications of acute suppurative otitis media and mastoiditis, and the mortality rate dependent upon these conditions have been diminished greatly.

Kolmer has said that "chemotherapy is not merely the treatment of a disease with chemical agents, that is as old as the art of medicine itself. Rather it is the treatment of disease produced by living pathogenic organisms with specific chemical agents or drugs capable of selectively destroying them without serious toxic effects." When a drug is found to be efficacious in the treatment of one type of infection, it does not necessarily follow that it will be of equal benefit in all infections. Yet such a discovery is prone to bring about indiscriminate and empirical use of the compound. This has happened to a great extent in the case of the sulfonamide drugs.

The new chemotherapeutic agents are not devoid of dangers in their administration and their usage should be governed by the results of careful investigation of the patient and the disease to be treated. First, one must weigh the possible benefit to be derived from treatment, against the dangers of administration of the drug.

In reference to acute suppurations in the middle ear and mastoid the following points must be considered. First, the oral administration of the chemotherapeutic drugs in acute suppurative otitis media and acute mastoiditis, and, second, the local use of the drugs in mastoidectomy wounds.

In the case of acute suppurative otitis media, the first question that must be answered is "which patients with this disease need chemotherapy?" It has been conceded by many otolaryngologists that over 90 per cent of cases of acute suppurative otitis media proceed to spontaneous resolution after an adequate and timely myringotomy. Now since the advent of the sulfonamide drugs most encouraging reports relating the marked decrease in the morbidity from acute suppurative otitis media and the reduction in the number of cases of surgical mastoiditis have appeared. Stuart, Bowers, Clem, Lindsay, Horan and French, Baker and Bradford, Galloway, and others have reported favorably on the treatment of acute suppurative diseases in the middle ear and mastoid by the use of these compounds. Long (12) has even suggested that chemotherapy might be used for 48 to 72 hours at the very beginning of an earache in an effort to prevent the development of a suppurative otitis media. Williams and his co-workers concluded that chemotherapy afforded the greatest protection against surgical mastoiditis when used in otitis media due to pneumococci. Osgood on the other hand advised against the use of chemotherapeutic drugs in conditions in which there is little or no mortality rate, and Lindsay emphasized the statement that "the treatment for a patient who is desperately ill is not necessarily a criterion of the best policy in the early stages of these infections or in a moderate or mild type of otitic suppuration."

Babcock seemed unwilling to admit that the decrease in the number of surgical cases of mastoiditis in New York was due solely to chemotherapy, and he indicated that the effect of this treatment in otitis media is somewhat overrated. Before subscribing to the practice of giving chemotherapy to every patient suffering from acute otitis media, one should analyze some of the

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extremely favorable reports of drug therapy. It seems that reported reductions in the number of cases of surgical mastoiditis may be somewhat misleading since many of the reported controlled groups demonstrate an extremely high percentage of cases of surgical mastoiditis. Let us attempt to determine possible causes for the fewer cases of surgical mastoiditis other than the direct effect of the sulfonamide drugs upon middle ear infections. Kopetsky has reported a distinct periodicity in the virulence of infection of the upper respiratory tract, particularly of the middle ear and mastoid, and has stated that in different years various subtypes of the hemolytic streptococci may be predominant. He suggested that a major cycle occurred about every 6 years.

Since chemotherapy has come to be used in a large number of patients with exudative nasopharyngitis, severe follicular tonsillitis and suppurative sinusitis with excellent results, many severe acute cases of suppurative otitis media probably have been prevented. This in itself has tended to reduce the number of surgical cases because these fulminating infections that spread to the middle ear eventuate in suppurative mastoiditis with relatively great frequency. Then there was that group of otolaryngologists who were prone to operate early in every case of severe otitis media which demonstrated fever, pain, profuse discharge, and mastoid tenderness. The more conservative aural surgeons had the courage to postpone surgical interference upon patients who demonstrated signs of uncomplicated mastoiditis in the first week of infection in the middle ear. This delay provided time for spontaneous resolution in the majority of patients and allowed walling off of the process in those who continued to develop a suppurative coalescent process in the temporal bone. Since the widespread use of chemotherapeutic agents in middle ear infections these early operations of which we know there was a tremendous number have been reduced to a minimum for the following reasons. First, the prevention of otherwise necessary operations due to the effect of the drug in the severe cases of acute suppurative otitis media. Here the acute infection in the middle ear was brought under control before extension to the mastoid had taken place. Second, and the exact importance of this factor cannot be determined, the prevention of unnecessary operations. The confidence in the sulfonamide drugs possessed by the patient, the general practitioner, the pediatrician, and the otologist, has acted as a deterrent to operation. The tempering of the acute symptoms has made the condition less alarming so that there has been no impatient cry for action

on the part of the patient, parents, or physician and many cases have been allowed to proceed to spontaneous resolution which might have taken the same course without the drug. If sound, watchful conservatism had been practiced.

Now, since prompt and excellent response to chemotherapy in severe acute cases of suppurative otitis media has been witnessed, why should not all cases of middle ear infection be treated routinely by the administration of one of the sulfonamide drugs. In answer to this question I wish to state that chemotherapy should be used scientifically and specifically with a definite objective in view. There is a morbidity and even a mortality rate attendant upon the use of these weapons which must not be ignored. If the object is the prevention of mastoiditis we are then considering a form of treatment which should not be given to over 90 patients unnecessarily in order to treat less than 10 who need it. Even though the drug were perfectly innocuous, such empiricism does not belong to the present era of scientific medicine. If the object is, and of course it should be where possible, to decrease the morbidity and to shorten the duration of the infection then a much higher percentage of patients with acute suppurative otitis media may be treated by these drugs. They should be selected on the basis of their general condition and the severity of the infection but should not be subjected to routine empirical treatment. The patient who has an infection severe enough to demand chemotherapy should be kept under close observation in order that the effect of the drug on the infection may be observed and the earliest signs of toxic reaction be detected. Those adult patients with mild acute suppurative otitis media treated by chemotherapy often insist upon remaining ambulatory and driving automobiles. The dangers attendant upon this are well known.

Finally the very significant number of patients who develop mastoiditis and intracranial complications insidiously during chemotherapy adds a new note of danger. The masking effect of the drug which allows these complications to develop without any alarming signs tends to give the physician a false impression of the patient's progress.

Allowing the sulfonamide drugs their very important place in the treatment of acute suppurative otitis media, which patients then with this disease should receive their benefits? Although it is difficult to draw any hard and fast rules, a few principles seem worth while to follow.

This treatment is best suited to those individuals in whom the disease is still a moruous men-

brane infection, and of course to those who have established and diagnosed complications of the suppurative process in the temporal bone. Bearing this in mind, chemotherapy should be used in the following types of cases

1 Acute fulminating infections in the middle ear producing signs of mastoid involvement at the end of the second or third day and characterized by sepsis, profuse aural discharge, pain and mastoid tenderness. In this type of disease there is frequently a spread of the infection by septic thrombophlebitis of the small communicating veins of the mastoid

2 Acute infections in the middle ear, either mild or severe, but secondary to a virulent process in the throat, nasopharynx, nose or paranasal sinuses. Chemotherapy in these cases may prevent a suppurative mastoiditis by controlling the primary infection

3 Early, acute, rapidly developing middle ear suppurations characterized by a red edematous tympanic membrane and thin seropurulent or serosanguineous exudate under pressure in the tympanum. This is the type of infection which may spread rapidly to the mastoid if not brought under control promptly

4 All cases of acute suppurative otitis media from which a pneumococcus is recovered on culture

In general only those patients who have an early acute suppurative otitis media without an established suppurative mastoiditis gain the greatest therapeutic effects from the drug. If suppurative mastoiditis has already developed, treatment will be less effective. Williams stated that "on the basis of review of literature in consideration of the mode of action of the drug, it would seem that the which good blood and oxygen supply are present, one which is free of peptones and broken down leucocytes and which is not constituted of bone. The middle ear and mastoid process are essentially bony loci with a notably poor blood supply." The condition in an infected mastoid is entirely different from that in an acute osteomyelitic process in the vascular red marrow of the metaphysis of a long bone. In the latter infections chemotherapy has started to revolutionize their treatment. Badgley reported 13 cases of acute osteomyelitis in the long bones treated by sulfathiazole. In each of 3 patients incision and drainage of soft tissues only was done and in 10 patients no incisions at all were made. All of these patients made splendid recoveries. With continued chemotherapy most otologists have witnessed infection in the mastoid proceed to intracranial involvement

Although one might offer as an explanation the difference in the types of bone in the mastoid and in the long bones, it has been our experience at the University of Michigan Hospital that spreading osteomyelitis of the skull, an infection in diploic bone, is not satisfactorily managed by chemotherapy alone. We still find it necessary to remove all infected bone and to expose a wide margin of healthy dura around the osteomyelitic process.

When sulfanilamide was the only sulfonamide drug available, it was usually advisable to know what organism was responsible for the infection before instituting therapy. This was due to the toxicity and the somewhat limited effectiveness of the preparation. Culture of the infecting organisms is still important and should be performed in every disease in which chemotherapy is contemplated, yet the newer drugs with wider scope of action and decreased toxic effects may be started before the culture has been completed. At the present time sulfathiazole is the drug of choice in most instances because of its effectiveness in combating infections due to hemolytic streptococci, pneumococci, and staphylococci. Sulfadiazine, which is now available, but rather expensive, bids fair to replace sulfathiazole as the preparation of choice in most of the infections encountered in an otolaryngologic practice. Long (13) has commented that it is the only one of the group of sulfonamide drugs that can be used in the home with relative safety.

The period of time during which chemotherapy should be employed in infections of the middle ear and mastoid has been the subject of controversial discussion. Bowers, Kolmer, Osgood, Lyons, Lindsay, and Williams, have dealt with the subject in some detail. Although it has been suggested by some that it might be advisable to wait for a few days after the infection appears in order to allow antibodies to develop before giving the drug, the general opinion now seems to be that treatment should be started immediately upon the appearance of the infection and that the dosage should be very heavy during the first day in order to gain a high blood level of the drug as soon as possible. Of course by the time a severe infection becomes manifest antibodies have already been produced to a considerable extent.

Since the greatest effect of the drug is to be gained when the infection is in the mucous membrane, or when there is being produced a septic thrombophlebitis of the small communicating vessels of the temporal bone, such therapy should be used during this period and then discontinued until further indications for its use arise. This

means that treatment should be given vigorously for 4 to 10 days, at the end of which time it has probably had its complete effect upon the early stage of the infection. Earlier discontinuance is indicated, of course, if important toxic manifestations appear. Failure of the infection to respond to therapy may indicate a lack of antibodies which should be supplied by transfusions or specific sera if available.

The indications for use of chemotherapy in the early stages of severe acute suppurative otitis media are more easily defined than are the indications in infections of the middle ear and mastoid of more than a week or 10 days duration. Empiricism must again be avoided in the latter group of cases and the drug should be used only after full consideration of each individual case. Although fever may be lessened and the objective signs of manifest bone involvement within the mastoid may be partially alleviated, the disease within the temporal bone is not likely to undergo spontaneous resolution at this stage if the patient is ill enough to demand chemotherapy. Because of the masking effect of the drug which may be due as suggested by Lindsay to a limitation of the infectious process, the otologist may be confronted by the insidious development of an intracranial complication.

Coalescent mastoiditis can and does proceed to develop on many occasions during intensive chemotherapy. Since this may happen rather quietly an especially alert vigilance must be maintained. Signs of the surgical mastoid are almost always present but are modified due to the lack of fever, pain, severe tenderness, and leucocytosis. The characteristic granular purulent exudate, sagging of the supraposterior canal wall, deafness, and progressive radiographic changes are present in most instances but are less imperative.

The local use of the sulfonamide drugs in infected and potentially infected wounds has been given a thorough trial in civilian and military surgery and has been proved to be of great value.

The postoperative care of mastoid wounds has changed from time to time in an effort to shorten the time of healing and yet assure adequate drainage. Many procedures varying from wide open drainage to primary suture after allowing the cavity to fill with blood clot have been suggested. More recently otologists have been using the sulfonamide drugs in the mastoid cavity in addition to regular gauze or rubber drains. Livingston had disappointing results from filling the mastoid wound with sulfanilamide crystals and then using the usual rubber drain and partial suture and believed that this procedure failed to shorten the

postoperative period. He reported 13 cases in which the wound was filled with either sulfanilamide or sulfathiazole and then closed tightly of which 11 showed prompt healing. Of the 11 patients so treated, the shortest healing time was 4 days and the longest healing time 9 days.

At the University of Michigan Hospital observations have been made by Dr. David DeWeese on 10 simple mastoidectomy wounds treated by the local application of sulfanilamide powder at the time of operation. The wounds were nearly filled with the powder and then the usual gauze packing was inserted. Wound cultures remained negative for streptococci until after the first dressing was done on the fourth or fifth day when streptococci and staphylococci began to appear. In 8 of the 10 wounds, no pus was seen until after the packing had been changed. The highest blood sulfanilamide level obtained was 0.45 milligrams per cent following the instillation of 10 grams of drug in the mastoid wound. The next highest blood level was 0.3 milligrams per cent and the remainder showed a very small amount of the drug in the blood. Although no conclusions can be drawn from this small group of cases, it seems certain that the effect of the drug upon the wound must be local and not the result of absorption. Also it might suggest that the wounds were reinfected in dressing them in spite of the fact that aseptic technique was employed in the procedure. Reinfection of the wound at the time of dressing is not the only explanation of the postoperative suppuration although this factor is important when any wound is dressed frequently. After a well done complete mastoidectomy there remains many small infected cells which may account for the reappearance of pus after the fifth postoperative day. Since some of these infected cells do remain it would seem that primary suture of the complete mastoid wound after the local use of the sulfonamide drugs is not an entirely safe procedure because provision is not made for open drainage. The local use of the drug, partial suture of the wound, and the use of a rubber drain that can be removed gradually without having to be reinserted probably offers the best type of dressing for the average complete mastoidectomy wound.

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RESULTS OF OPERATION FOR HETEROPHORIA AND HETEROTROPIA AND CAUSES OF FAILURE

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THE subject of heterophoria and heterotropia may be discussed from several viewpoints I have chosen to discuss it in relation to the type of operation indicated or contraindicated according to the diagnosis. There may be some who do not yet think of squints and phorias as having *definite* surgical indications, depending upon an accurate diagnosis. The subject of diagnosis has already been discussed by my distinguished colleague Dr White.

THE HETEROPHORIAS

The heterophorias may be divided into the esophorias and the exophorias. The esophorias may be mechanical, accommodative, or mechanical plus accommodative, the mechanical or essential esophoria may be due to convergence excess or to divergence insufficiency.

Essential esophoria due to convergence excess is curable by surgery, it may possibly be symptomatically alleviated by other means but not cured. When due to convergence excess a lessening of the action of the median rectus or recti will result in a permanent cure. If it be due to divergence insufficiency, operation upon the median rectus will not only fail to relieve the esophoria but will permanently disable the convergence and the condition will be worse than before. We have found the Jameson recession operation to be eminently satisfactory, only one median rectus being recessed at a time.

The cure of this form of esophoria may be achieved only by proper surgery. It may require a procedure as extended as that for the cure of

convergent squint of the same type. A lapse of some months should be allowed after the first operation before an operation is done upon the median rectus of the fellow eye, should this be necessary.

In mechanical esophoria due to divergence insufficiency shortening of one or both lateral recti will result in a permanent cure. Obviously, the extent of the shortening will depend upon the degree of the esophoria. Careful study and understanding of the case enables the surgeon to judge as to the extent of the operation. When properly performed as to surgical technique and with a full understanding of the surgical requirements in the particular case at hand, the result will be eminently satisfactory in a very large majority of the cases. Naturally, no surgical procedure is satisfactory in all cases. In a case of esophoria due to divergence insufficiency, operation upon the median recti is contraindicated.

It is unfortunate to put glasses upon a patient with mechanical esophoria since they have no effect whatever upon the degree of the esophoria. In a purely mechanical esophoria it will be obvious upon reflection that correction of the refraction will not alter the degree of the esophoria and hence will not relieve the patient. Only if there be an accommodative factor will the degree of the esophoria be lessened.

Regarding accommodative esophoria, or functional esophoria, I wish to emphasize the following statement. In purely accommodative esophoria, surgery is absolutely contraindicated. If operation is done, the result will be an exophoria for distance and an esophoria for near. The esophoria will probably develop into a divergent squint for distance with an esophoria for near.

It is improper to prescribe glasses for permanent wear. They do not cure an accommodative exophoria but correct it only while the glasses are being worn. This is symptomatic treatment only and is unsatisfactory. Accommodative exophoria can be cured by dissipation of the accommodation and convergence by proper orthoptic training.

In combined mechanical and accommodative exophoria, the mechanical factor requires surgical correction according to the suggestions made. The accommodative factor is amenable to orthoptic training as mentioned. An accurate diagnosis before treatment is attempted is essential.

The exophorias may be mechanical, accommodative, or mechanical and accommodative. In mechanical exophoria due to convergence insufficiency surgery is necessary. Proper correction of the myopia, together with orthoptic training to correct (1) the convergence insufficiency (2) to improve fusion to a wide amplitude, and (3) to obtain third degree fusion or stereopsis, may give satisfactory functional results but will not cure the exophoria.

To obtain a permanent cure, shortening of the median rectus or recti is indicated. The results are not so satisfactory as in esophoria. Relapses are more frequent. Judgment is more difficult as to the degree of shortening indicated. A primary overcorrection is desirable.

The results are often not entirely satisfactory. Bkelschowsky suggests it is better to wait until adolescence before operating in such cases. Our experience justifies this. Careful study of the patient, patience and an understanding of the many factors involved will enable the surgeon, with proper surgical measures, to obtain a satisfactory cure in the majority of cases.

It is my impression that in the presence of mechanical exophoria due to divergence excess, more brilliant successes are obtained by means of surgical treatment in this condition than in an other motor anomaly of the eyes.

Lessening the action of one lateral rectus at a sitting followed by a similar procedure on the fellow eye after the proper interval of time has elapsed results in a permanent cure more certain than does that secured by any other surgical procedure. The Jameson technique, recessing one lateral rectus 4 to 5 millimeters, appears to us to be the ideal operation. It is unsafe to recess both at one sitting, and it should not be done.

Exophoria of more than 8 prism diopters for distance prevents entrance of recruits into the commissioned personnel of the armed services, the air corps, or commercial flying. The surgical

cure is so easy and so eminently satisfactory that no person should be deprived of the inestimable benefit of correction. In selected cases and under proper conditions, the patient will not have to remain in the hospital but may resume his duties within 24 hours.

Mechanical plus accommodative exophoria is usually an exotropia and will be discussed under that heading.

Accommodative exophoria is the result of myopia. The myope of 2 or 3 diopters or more uses no accommodation for near work and hence little or no convergence. In consequence such a patient develops an exophoria which very soon becomes an intermittent exotropia at which time there begins to develop a mechanical factor.

A purely accommodative exophoria does not indicate surgery. Cure can be obtained by correction of the refraction and orthoptic training.

SQUINT

Squint may be convergent or divergent.

Convergent squint may be (1) mechanical (a) due to convergence excess, (b) due to divergence insufficiency (c) due to convergence excess plus divergence insufficiency (2) accommodative or (3) mechanical plus accommodative.

Divergent squint may be (1) mechanical (a) due to convergence insufficiency (b) due to divergence excess, (c) due to convergence insufficiency and divergence excess (2) accommodative (3) mechanical plus accommodative.

Convergent mechanical squint due to convergence excess is not benefited by glasses. Orthoptic exercises alone will not correct the squint, if it does so the squint is not a mechanical one. Surgical treatment is indicated and should aim to lessen the action of the median rectus or recti. In this form of squint we have found that the Jameson recession operation, properly used, gives eminently satisfactory results. To secure a functional cure in such cases, 3 factors are necessary: (1) absolutely accurate diagnosis (2) knowledge of how much to recess the median rectus or recti, (3) efficient orthoptic training to secure fusional amplitude and stereopsis. The causes of failure are obvious, the most important of which are incorrect diagnosis and consequent improper surgery uncalculated for or an improper surgical procedure will result in failure. Shortening or advancement of the lateral rectus or recti is contraindicated and will result in an unsatisfactory result or failure.

The surgical treatment in mechanical convergent squint due to divergence insufficiency should be directed to the lateral recti. We seek to in-

crease their action by advancing, shortening, or both, by any operative procedure the surgeon prefers or in which he is most adept. The par-ticular operation is of no great moment, but the choice of operation is essential to success. Error in this choice will cause failure, partially or com-pletely. To operate upon the convergence muscu-lar system when the divergence only is involved, will cause tragic failure since the squint will not be relieved and the convergence will be weakened. This adds to the cosmetic failure, a weakened con-vergence which may cause great trouble.

Surgery is absolutely contraindicated in purely accommodative convergent squint. Cure can be secured in such cases only by orthoptic training. If operation is done there will be a divergent squint for distance. The result of surgery in such cases is tragic failure and renders such eyes ab-solutely incurable for all time.

In accommodative mechanical convergent squint the mechanical factor should be corrected by surgical means, the accommodative, by or-thoptic training. Before operation is done to cor-rect the mechanical factor, due regard should be given to the question whether the squint is the result of convergence excess or divergence in-sufficiency as above discussed. Failure to observe this or failure to recognize the accommodative element will bring about unsatisfactory results.

In cases of mechanical divergent squint it is unusual to find a patient without an accommo-dative factor, the majority have myopia. Biel-schowsky advised that no operation be done to correct divergent squint before the adolescent age because of the possibility of recurrence. This judgment was no doubt formed in Germany. In our country conditions are so different that this would not seem to be proper judgment here. Be-cause of the adverse effect on the mental develop-ment of a child, any squint should be corrected and cured at the earliest possible moment.

Mechanical divergent squint requires surgery for a cure in the following instances

a When due entirely to convergence insuffi-ciency shortening of the median rectus or recti is necessary. Considerable experience is necessary in order to determine the degree of shortening or advancement or both that may be required. When combined with orthoptic training to over-come suppression, which is almost always present, the results are good. Recession of the lateral rectus or recti may be necessary in high degrees of divergence in addition to shortening of the median rectus. Overcorrection is required since there is a strong tendency for the squint to recur. In our experience correction of a mechanical divergent

squint is more difficult and less satisfactory than that of convergent squint. The patient should be informed that recurrence may occur and that further surgery may be required. Suppression which is likely to be intermittent is difficult to overcome, consequently extended orthoptic train-ing may be required and the case kept under ob-servation over a long period.

b Surgery is necessary in mechanical divergent squint due entirely to divergence excess. One rarely finds such a case. Often exophoria is due purely to divergence excess but by the time it has become an exotropia there is usually added con-vergence insufficiency. In a case with pure diver-gence excess, recession of one or both recti gives a most satisfactory cure which is often permanent, provided there is no convergence insufficiency or the anatomical anomaly is not so great that recur-rence is likely. Obviously orthoptic training and correction of the refraction are concomitant neces-sities in obtaining a cure. May I emphasize the word *cure* which means binocular vision with stereopsis. Without this the case is only cos-metically corrected not cured.

In the great majority of cases of divergent squint due to divergence excess plus convergence insufficiency, a high degree of resection and ad-vancement of both median recti may be required, possibly combined with recession of the lateral recti. A cure is not always possible though a cos-metic correction may be secured. The advanced muscle detracts from the cosmetic result. Limita-tion of abduction may result even though both eyes are operated upon. This is undesirable but may be necessary in correction of ocular deformity.

The causes of failure of correction appear fre-quently to be an insufficient degree of resection and advancement primarily to overcorrect the squint. Extreme limitation of movement of one eye may result from too great shortening of the median rectus with or without recession of the lateral rectus. The correction necessary in the higher degrees of squint should be equally dis-tributed between the two eyes. An excess correc-tion may result in convergent squint which may cause an annoying and possibly an insuperable diplopia. One should proceed with caution in high degrees of alternating divergent squint. Correction of the deformity may result in diplopia, so annoying to the patient that it cannot be endured. We believe such cases to be very rare and have not hesitated to correct such squints. We have had no case of serious diplopia following surgical correction.

Accommodative divergent squint differs in many respects from accommodative convergent

squint. It is the beginning of the mechanical form and results from myopia. The child is myopic and uses no accommodation for near vision consequently no convergence. He fixes with one eye and the other is relatively divergent. Hence suppression occurs for near vision which is therefore intermittent suppression. Slight amblyopia may occur which later becomes more marked as the squint progresses from an intermittent to a constant one.

The child has a divergent squint only for near at the beginning, hence it is functional i.e. accommodative. The child, however, only squints when he is looking down, that is, in near work. Consequently it is not observed by the parents. Very likely his myopia will not be discovered until he goes to school. By this time the squint will probably have a mechanical factor in addition to the accommodative factor.

It is obvious that we rarely see a purely accommodative divergent squint. It is equally obvious

that surgery is not indicated if the case be entirely accommodative. Correction of the refraction and orthoptic training will be adequate to establish a cure in such a case.

In mechanical plus accommodative squint surgical correction and in addition orthoptic training and correction of the refraction are required. Surgery properly adapted to the particular case is usually satisfactory and a cure is accomplished in conjunction with the other treatment mentioned. The degree of squint is usually not great and there should be no failures in such cases. Failure could come only from improper diagnosis and poorly conceived or improperly performed surgery.

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OTOLOGICAL SYMPTOMS OR COMPLICATIONS OF CRANIOCEREBRAL INJURY

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WITH the accelerated pace of our industrial life and with war rampant in the world, there are an ever increasing number of head injuries. With the exception of headache, the most frequently encountered symptoms of head trauma lie in the field of otology.

The anatomical considerations are briefly these: the external ear, external canal and membrana tympani, the middle ear, the cochlea and vestibule, the cochlear and vestibular nerves, the facial nerve, the first way stations of cochlear and vestibular nerves in the floor of the fourth ventricle and brain stem, and the central cochlear and vestibular connections.

In the production of intracranial damage the head may strike an object, be struck by an object or be violently jarred against the vertebral column. In considering the mechanics of such an injury there are three distinct phases: (1) the moment of impact, (2) the movement of skull and brain, (3) the cessation of skull movement. As the brain floats freely in the cerebrospinal fluid and as there is a certain element of inertia in its movement, it can be damaged by impact against the inside of the skull in either the first or the third phase of the injury. Such damage, when it occurs in the third phase, is of the contre coup variety.

As to the type of pathology produced, there may be fractures of the skull with concomitant brain injury or brain injury without any demonstrable skull fracture. Fractures of the skull may involve the facial bones, the vault, the base, or any combination of these. Fractures of the base constitute from 60 to 80 per cent of all skull fractures. They may involve the anterior, middle or posterior fossae, but those involving the middle fossa predominate. They may be of the bending or bursting type.

Fractures of the temporal bone, which is very loosely fitted into the base and which constitutes a large portion of the middle fossa, occur whenever the middle fossa is fractured. Transverse fractures of the temporal bone, which cross it more or less at right angles and destroy its contents.

tents, are initiated in the posterior fossa. The contents of the temporal bone may also be damaged by violent swinging movements of the temporal bone without any fracture having taken place. In the vast majority of cases, a transverse fracture of the temporal bone causes a complete cochleovestibular paralysis, but there are a few well authenticated cases in which a portion of either the cochlear or the vestibular function is spared.

Another type of injury of interest to the otologist is injury to brain tissue, particularly pathology involving the brain stem and the region of the floor of the fourth ventricle where it can damage the cochlear and vestibular nuclei and their central connections. Such pathology consists of contusions and petechial hemorrhages, the tearing of blood vessels, the tearing, stretching, and laceration of cranial nerves, and damage to the vasomotor center and vasomotor nerves resulting in irritation of the vestibular nuclei.

A third type of injury which is of peculiar interest to the otologist is the direct injury to the cochlear and vestibular end organ. This is occasioned by transverse fractures of the otic capsule which actually destroy the sensory epithelium, by longitudinal fractures of the temporal bone which do not of themselves invade the capsule but which are associated with bleeding into the basal coil of the cochlea, by the tearing or stretching of the eighth nerve at the internal auditory meatus and by wave movements of perilymph and endolymph caused by violent swinging movements of the entire pyramid.

Careful history taking is of importance in evaluating a head injury. In general it may be said the older the patient the more serious are the effects of the injury and vice versa. The baby's skull, because of its great elasticity, absorbs the effects of trauma very well. The question of unconsciousness is an interesting one. In general it may be said that the longer the period of unconsciousness the more serious the injury. And yet we encounter rather serious intracranial damage in cases in which no loss of consciousness occurred. A truck driver walked into my office a few weeks ago complaining of headache. Ten days before, while closing the rear doors of his truck he fell

backward, striking his head against the pavement. He continued his work as a truck driver until he consulted me. Examination revealed a linear fracture of the occipital bone about 4 centimeters long. At no time was he unconscious.

Bleeding from the mouth, nose, or ears generally indicates a basal fracture. It may come on immediately but in some cases it may be delayed for a couple of days or even up to a 2 week period. The history of any previous injury to the head is of value in evaluating the signs. Any information as to the previous condition of the cochlear or vestibular apparatus is of vital importance.

In the examination of the patient, the importance of team work between the surgeon, neurologist, ophthalmologist, and otolaryngologist cannot be stressed too strongly. Otological examination divides itself into immediate, as soon after injury as possible and subsequent examinations.

The immediate examination of the patient should concern itself with the following points: presence or absence of consciousness; presence or absence of facial paralysis or weakness; presence or absence of ptosis or strabismus; condition of the pupils and pupillary reflexes. The otoscopic examination will disclose any blood or cerebrospinal fluid in the external canal, any bloody crusts, fissures or cracks in the canal wall, any rupture of the drum or the presence of hematotympanum. Rough hearing tests should be made as soon as the sensorium of the patient permits to determine qualitatively if hearing is present. The presence or absence of spontaneous nystagmus in different positions of the eyes should be noted, especially if there is a complaint of dizziness. If the patient is unconscious, a conjugate deviation of the eyes can often be seen. This has the same significance as a spontaneous nystagmus in the conscious patient.

Subsequent examinations will concern themselves with a study of all the cranial nerves. The sense of smell should be investigated. The eyes should be studied in regard to pupil size and reaction, action of the extraocular muscles, media and fundi, diplopia and the field of vision. The action of the facial nerve should be carefully investigated. The hearing function should be examined by the voice, tuning fork reactions, and the audiometer preferably in a sound proof room. A study of the vestibular mechanism should include all the spontaneous signs of vestibular disturbance as well as the induced vestibular reactions, both thermal and rotatory.

SIGNS AND SYMPTOMS

The signs and symptoms which especially concern the otologist are tinnitus, loss of hearing,

dizziness, the escape of blood or cerebrospinal fluid from the ear, the presence of facial paralysis or weakness, the presence of fracture lines in the external auditory canal, and the development in 4 to 5 days of Battle's sign, ecchymosis over the mastoid process.

Spontaneous vestibular vertigo is subdivided into turning or rotatory vertigo and tactile vertigo. In turning vertigo the patient will indicate in some way that either he feels himself turning, the more common variety or that objects in his environment are rotating, not so common. There is no more certain sign of vestibular disturbance than turning vertigo. Tactile vertigo is again divided into (1) errors of sensation and (2) lateropulsion. In lateropulsion, which is not very common, the patient feels himself being pushed to one side.

The patient with an error of sensation has a feeling of tilting or tipping, of uncertainty or unsteadiness, or he complains of faintness or spots before his eyes. He does not experience any sense of rotation. His vertigo is not accompanied by spontaneous nystagmus, but his vestibular mechanisms usually show unequal responses to thermal stimulation.

Unless there has been a complete cochleovestibular paralysis caused by a labyrinthine fracture the vertigo is not constant but comes on in bursts initiated by sudden movements of the head, bending, lifting, exposure to sun and heat, elevation above ground level and indulgence in alcohol.

The spontaneous signs of vestibular disturbance are of more importance in checking for brain stem pathology than are the induced reactions, induced by either the caloric test or the rotation chair. These spontaneous signs are nystagmus, past pointing, drift in the deviation test, gait deviations, the Romberg test, and the girdle reactions.

Spontaneous nystagmus due to vestibular disturbance is a jerky nystagmus. It is usually rotary and horizontal. If vertical or diagonal in character it may be due to a brain stem lesion but it is not vestibular in origin. After a total exclusion of the labyrinth, it is continuous but if due to pathology in the region of the vestibular nuclei, it is intermittent. It may appear in all three positions of the eyes, but if mild in degree, will only be seen if the eyes are turned in the direction of the quick component. It should be searched for in every position of the head and eyes with the head erect, head tipped backward and then forward, and with the head tipped to either shoulder the so-called positional nystagmus. If no nystagmus is seen in these positions, it can sometimes be made to appear by rapidly

shaking the head, the so-called "head movement test." This test will not produce a spontaneous nystagmus in a normal individual. If a spontaneous nystagmus is intermittent in character, do not expect to find it on every examination and do not make the mistake of saying that there is no spontaneous nystagmus present in a patient from one single examination. The nystagmus will only be present on those occasions when the central vestibular nuclei are being irritated and when the patient has a subjective sense of rotation. This also applies to the other spontaneous signs of vestibular disturbance.

If a patient has a subjective sense of rotation, he will past point when the pointing test is made in the vertical plane, his outstretched arms will drift to the right or left in the deviation test of Fischer and Wodak and he will deviate to one or the other side when he walks forward or backward with eyes closed.

If the patient has a sense that he is tipping or tilting, he may past point if the pointing test is made in the horizontal plane.

The falling reaction is best tested by the Romberg test. I shall not try to describe to you the technique of performing the Romberg test. Suffice it to say that when making the test in a medicolegal case, every effort should be made to divert the attention of the patient while the test is made. If a falling tendency is due to a peripheral labyrinth lesion, the fall will be in the direction of the slow component of the existing spontaneous nystagmus, no matter which way the head is turned. If the lesion producing the positive Romberg is central, it may still be vestibular in origin and then the fall will be in the direction of the quick component. If the lesion is cerebellar, the fall will be always backward or forward if the vermis is affected and always to the same side if one of the hemispheres is affected, and this fall bears no relation to the position of the head or any pre-existing nystagmus.

As I mentioned previously, I consider the spontaneous vestibular signs as more important than the induced reactions, but at times it is necessary to employ the induced tests. One can use either the turning chair or thermal stimulation, the caloric test. The turning chair has the disadvantage that it stimulates both labyrinths at the same time and, for this reason, I prefer the caloric test. Unless I am testing the peripheral labyrinth for total exclusion, I prefer to use the so-called minimal stimulation method. I slowly introduce 5 cubic centimeters of water at 80 degrees F into the external canal after having tipped the head back 60 degrees. This so-called optimum posi-

tion is used because the horizontal canals are thus put into a vertical position and we know that the horizontal canals stimulate thermally more easily than do the vertical canals. In anywhere from 10 to 25 seconds a nystagmus appears while the patient is looking straight forward, which nystagmus lasts from 1 to 2½ minutes. If the two ears exhibit a greater difference in the latent period than 5 seconds, or if there is more than 30 seconds difference in the duration of the induced nystagmus, we feel that the two vestibular mechanisms are not in balance. Fixation on the part of the patient should be prevented by the use of strong convex lenses. This minimal stimulation serves very well for studying the induced nystagmus, but is not strong enough to study induced pointing and falling reactions. It rarely produces nausea or vertigo except in the hysterical type of patient. It is needless to say that the caloric test cannot be used when there is a pre-existing spontaneous nystagmus in the central position of the eyes, nor is it of any value under these conditions.

The hearing of the patient should be tested by the voice, tuning forks, and audiometer. Bone conduction should be investigated in the Rinne and Schwabach tests. The audiometric test should preferably be done in a sound proof room. Qualitative hearing tests should not be made until the sensorium of the patient has cleared and preferably not until he is up and about. The audiometer has the advantage that it produces relatively uniform and relatively pure tones and that a graph can be made of the entire range of hearing, which can be compared to subsequent graphs and also, to some extent, to audiometric examinations made by another. Its disadvantage is that a diagnosis of the type of deafness cannot be made by its use alone. For this it must be supplemented by the use of tuning forks.

Loss of hearing due to head trauma can result from the effects of brain contusion alone, without any fracture of the cranial bones. It may result from a longitudinal fracture of the temporal bone, which courses along its anterior edge and projects itself into and through the tympanic cavity. It may also result from a transverse fracture of the pyramid which destroys the sensory epithelium of the cochlea and causes complete loss of cochlear function. Unless there has been an actual fracture of the labyrinth, in which case the loss of hearing is usually complete, the predominant type of deafness produced by a blow to the head is a perceptive or high tone deafness, associated with shortened bone conduction and a strongly positive Rinne reaction. Even in those cases in which there has been a fracture of the cranial bones

ther than a direct fracture of the labyrinth this type of hearing loss is due in large measure to the effects of hemorrhage into the labyrinth and not to the actual fracture itself. It has been proved in experimental animals that a blow to the head of insufficient force to fracture the skull will produce hemorrhages into the perilymph spaces of the basal coil of the cochlea and the harder the blow the farther up in the cochlea will these hemorrhages extend. Some of this blood will absorb, but often it produces a perceptible type of deafness.

When a fracture courses through the middle ear ruptures a drum, and damages the intra-tympanic structures in addition to producing the previously mentioned high tone loss, a combined type of deafness might be expected. However when the ruptured drum closes and the fracture through middle ear heals, recovery of hearing in lower and middle tone ranges is often truly remarkable.

ROENTGENOGRAPHY

The roentgenographic delineation of basal skull fractures in general, with one exception, is very difficult even when the skull is photographed from every conceivable angle. The roentgenographic examination should include antero-posterior, lateral, oblique, vertex, mental, and Stenvers' exposures. Stereoscopic views are very useful. Even when all of these views fail to reveal a basal fracture one is not justified in saying that it does not exist. Hemorrhage from the mouth or nose, suffusion about the eyes and the roof of the nose, a slowly developing ecchymosis over the mastoid, the escape of blood or cerebrospinal fluid from the ear and the presence of hemato-tympanum are suggestive of basal fracture even in the absence of roentgenographic confirmation.

The presence of a large amount of endocranial bone in the otic capsule, bone which shows little or no tendency to regenerate permits of the roentgenographic delineation of a labyrinth fracture many years after its occurrence. So it may be said, in contradistinction to the usual failure to demonstrate basal skull fractures roentgenologically, that fractures through the petrous pyramid can almost always be demonstrated.

FACIAL PARALYSIS

Facial paralysis may be caused by longitudinal or transverse fractures, by nerve injury by stretching or tearing at the internal auditory meatus, or by hemorrhage into the fallopian canal. It may come on immediately or be delayed as long as a couple of weeks. It may be complete or partial. It complicates 10 to 15 per cent of all longitudinal fractures and about 50 per cent of all

transverse fractures of the pyramid. Surgery is not indicated for this condition. Unless this complication has been caused by a transverse fracture of the petrous pyramid recovery is the rule.

PROGNOSIS AND COMPLICATIONS

The immediate mortality from basal skull fractures is high, amounting to as much as 53 per cent according to various statistics. Late meningitis accounts for from 7 to 8 per cent mortality. The fractures of the otic capsule do not close by bony callus and, therefore, the late development of meningitis is encouraged when a mild otitis media ensues, even many years after the injury.

Most of the cases presenting a blood or cerebrospinal discharge from the ear recover without the development of meningitis unless the otic capsule itself has been fractured, and unless suppuration ensues.

TREATMENT

The principles in the therapy of cranio-cerebral injuries can be rapidly summarized. The first consideration after injury is the treatment of shock by bed rest, elevation of the foot of the bed, warmth, the use of shock cabinets, etc. The appearance of cerebral edema is discouraged by dehydration. This is accomplished by the limitation of fluid intake by the use of magnesium sulphate, and by intravenous injections of glucose or sucrose. Morphine tends to increase cerebral edema and should not be used. Craniotomy should not be encouraged unless there is evidence of increasing cerebral edema or a lapse into unconsciousness after a lucid period, indicating hemorrhage from the middle meningeal artery.

Any manipulation of an ear discharging blood or cerebrospinal fluid should be discouraged as it may result in suppuration and subsequent meningitis. This cannot be stressed too strongly. Such an ear should be covered by sterile dressings which should not be disturbed for several days.

If a bleeding ear suppurates and there is no evidence of a capsular fracture, it may safely be treated as any other otitis media. A fracture of the otic capsule will be recognized by the total deafness produced. If a fracture occurs through a chronically discharging ear a radical mastoid operation should be done as soon as patient is out of shock and fracture line should be exposed. If ever after a transverse fracture of the pyramid, a middle ear suppuration should supervene, a radical mastoid operation should be done at once.

Needless to say the advent of chemotherapy has markedly brightened the prognosis of ear suppuration developing after basal skull fractures involving the temporal bone.

INTRACRANIAL INFECTIONS AND THEIR SPREAD FROM THE EAR AND THE NASAL ACCESSORY SINUSES

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IT always seemed poignantly dramatic in our student days to be told that there were seventeen pathways along which infection might travel from the temporal bone to the meninges and we trembled with fear at the thought of germs in the tympanum or mastoid that could choose so many avenues of attack. On an anatomical basis the unfortunate individual with a suppurative process in the middle ear and mastoid bone had a poor chance for his life. With the intracranial cavity the terminus of seventeen routes through the temporal bone, it appeared inevitable that the invading organism would find its way to the meninges and there establish a process that only a decade ago was a little less than 100 per cent fatal.

But as our clinical experience grew and furnished us practical information on the behavior of temporal bone infections, we discovered that our fears were unnecessarily exaggerated and largely unfounded. Experience did not confirm the supposition derived from anatomical study. Infection did not usually extend without restraint along the many avenues of approach to the brain but on the contrary frequently remained within the middle ear and mastoid for weeks and even months without evidence of spread beyond the confines of bone.

The usual course pursued by an inflammatory process in the temporal bone or within the nasal accessory sinuses that gives rise to an intracranial complication is one which causes a destruction of tissue by continuity of infection and ultimately reaches the subarachnoid space by direct extension through the dura mater. To be sure, there are common exceptions to this rule. We have all witnessed the tragedy of a meningitis following on the heels of a fulminating acute ear or sinus infection several hours or a few days after the onset of the disease. Or, we have witnessed the development of a septic thrombus in the lateral sinus and rapid invasion of the meninges from this source within 4 or 5 days after the first signs of an inflammatory process in the middle ear. Intracranial complications of this type are obviously due

to a hematogenous dissemination of infection either in the form of a rapidly developing arteritis or phlebitis or the dissemination of septic emboli to the vessels of the meninges.

In discussing this precipitous variety of meningeal infection which, as has been implied, occurs less frequently than the more insidious and delayed form, particular emphasis should be given to the intracranial complications of the swimmer. From my point of view the acute fulminating sinusitis which develops after swimming is fraught with dangerous potentialities. There is an inordinate tendency in these cases for the infection to spread rapidly within 2 or 3 days to the intracranial tissues and to establish a diffuse meningitis or brain abscess. The precise mechanism of such an invasion is the subject of ethical differences of opinion to autopsy, it was obviously due to a retrograde thrombosis of the veins of the mucous membrane of the frontal sinuses which communicate with the dense plexus of veins in the coverings of the brain. In the cases of acute sphenoiditis there were instances of cavernous sinus thrombosis with the characteristic signs and symptoms of this disease and subsequent involvement of the meninges or brain. The point is that sinusitis in the swimmer is a dangerous disease, when it invades the intracranial structures it is prone to do so rapidly and to produce a complication of serious proportions in an uncommonly short period of incubation.

All of which has given rise to a great deal of speculation and considerable acrimonious dispute on the therapeutic management of these cases. There exists a school that, for reasons which appear sound to its advocates, recommends immediate tapping of the frontal sinus with a drill through its floor or anterior wall in an effort to establish early drainage of the purulent collection. There is another group who for equally good reasons is unalterably opposed to this point of view. As for myself, I have long held to the dictum, a void bone work in the presence of a green infection. Do not interfere surgically with a sinus involved in an acute inflammatory process. The rationale of this admonition would give rise to a discussion that is beyond the scope of this paper, suffice it to say that we are alarmed at the frequent occurrence of

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diffuse osteomyelitis of the skull after surgical attack upon an acute nasal accessory sinus disease. In our series of 84 cases of osteomyelitis of the calvarium, the disease developed after bone work had been done in 52 cases of acute sinusitis or acute exacerbations of a chronic infection. The high incidence of this devastating disease under these circumstances would seem to point to some error of commission or omission on the part of the surgical procedure rather than to a matter of mere accident or coincidence. Consequently it is axiomatic in our clinic to treat an acute sinusitis conservatively and to limit our surgical efforts to soft tissue drainage when the infection has perforated the walls of the sinus. Bone interference is resorted to only in the subacute or chronic stages of the disease. It is amazing and likewise gratifying to observe how frequently the acute sinus sufferer will recover spontaneously if he is given a narcotic for his pain, a shrinking solution for his nose and incision for the purulent collection that occasionally develops in neighboring tissues.

But there is another cogent reason for skepticism concerning the value of early sinus drainage by drilling through its walls, namely the doubt that the operation can be instituted before the intracranial complications intervene. Reference has already been made to the rapid occurrence of meningitis in the sinusitis of the swimmer. There are instances by no means rare when the sinus disease and the meningeal infection seem to occur almost simultaneously. One follows the other at such a rate as to preclude the possibility of instituting a surgical measure in time to prevent invasion of the meninges. At the risk of evoking bitter criticism, I should like to pose the opinion that when the surgeon opens a frontal sinus in the acute sinus disease of the swimmer he is usually too late to prevent an intracranial complication that was destined to occur from the onset; moreover, if the patient who has been subjected to surgical drainage does not develop a meningitis or brain abscess, there is still no justification for the assumption that the operation served as a preventive measure. Specifically I do not believe that the end justifies a surgical means.

Come now to the discussion of another method of spread of infection to the intracranial structures, attention is called to extension by continuity and contiguity of tissue. In our experience this would appear to be the common form of invasion when the inflammatory process has progressed to the subacute or chronic stages. The infection remains active within the sinuses or temporal bone for weeks or even months, destroys the surrounding osseous tissues, and finally reaches

the coverings of the brain. The dura, although a highly resistant connective tissue membrane may ultimately succumb to the ravages of the disease. Its invulnerability to infection, however is often amazing. An inflammatory process of uncommon virulence may grow on its surface for many months producing a large extradural abscess with pressure retention beneath the inner table of the skull without invasion of the intracranial cavity. Finally however the fibers of the dura may liquefy and open the subarachnoid space, an intracranial sinus, or the brain to the inflammatory process.

It is interesting to observe that a brain abscess derived from a nasal accessory sinusitis, a temporal bone infection, or an osteomyelitis of the calvarium that has passed beyond the acute stages is usually the result of direct extension to the cerebral cortex. An abscess stalk marks the line of invasion, within which it is clearly seen that the brain is attacked through a perivascular infiltration. The stalk is the result of a fibrous connective tissue proliferation and many new formed blood vessels. An infiltration of the perivascular spaces is much in evidence and it is by means of this pathological process that the infection is carried into the deeper parts of the brain.

Thrombosis of the cerebral vessels is occasionally observed in postmortem material but it is by no means the predominant method of spread. Infection from chronic inflammatory processes in neighboring bone does not frequently extend to the brain in this manner. A thorough search of many brain abscesses derived from such sources seems to indicate that the prevailing method of diffusion of infection is by perivascular infiltration and not through the migration of septic thrombi within the pial and cerebral veins.

It is to be remembered however that the point of entrance of infection into the cranial cavity may be widely removed from the primary focus within the temporal bone or nasal accessory sinuses. Anatomically it may be clearly demonstrated that the veins of the mucous membranes of these regions communicate directly with the dural vessels. It can be shown further that these veins may become involved in a septic thrombophlebitis which tends to distribute infection to remote regions of the dura. The typical pathological change is that of a septic exudate spreading over the surface of the dura beneath the intact inner table of the skull and frequently extending far beyond the original site of infection. Occasionally this exudate is found in one or more isolated patches under the calvarium and separated from the primary focus in the accessory sinuses or the mastoid bone by a

zone of healthy dura. Notwithstanding this mode of diffusion access to the intracranial cavity, when gained, is usually by direct extension from the extradural abscess which is virtually an extradural abscess through the fibers of the membranous coverings of the brain.

TREATMENT

that have a specific effect upon bacteria, there was always some question in my mind as to the value if any, of a mastoid or a sinus operation upon the victim of meningitis. Because it seemed to be in accord with the best principles of surgery and to hold out the only hope for a cure, we routinely operated upon these patients in the early years of our experience. But the results were most discouraging. Death was inevitable in spite of our efforts and after many disappointments the futility of this practice was realized and operative procedures abandoned.

With the advent of chemotherapy and surprising recoveries from meningitis, there has been a renewal of the orthodox method of treatment and renewed confidence in the practicability of surgical intervention. Once there appeared to be some hope for the life of the patient there came a strong resurgent interest in the time-honored principle of eradicating a focus of infection that was the cause of a complication. Cut off the source of supply of the crani and this practice seems to have captured the approval of otologists everywhere today. So we now advocate the eradication of an infective process and mass drainage of the products of inflammation by the radical removal of necrotic bone in conjunction with adequate doses of the sulfonamide drugs.

Reference has already been made to the predominating method of diffusion of infection to the brain by perivascular infiltration and in this connection we find a lesson, I believe, of some practical value. Where brain abscess is suspected it is rational to assume that the pathology of spread has been direct and therefore to search for the area of softened dura through which the disease has passed. Careful and meticulous removal of the exudate from the dura will frequently disclose the portal of entrance and give access to the pathway along which the infection has traveled. Gentle penetration of this region with a brain cannula often produces a drop of pus and reveals the identity of the inflammatory stalk. Thus we may enter and drain the abscess through a tract along which the infection has migrated and in so doing respect a surgical principle which in no other part of the body can be more advantageously applied.

At the risk of pointing out the obvious, your attention is called to the great value of chemotherapy in the treatment of ear and sinus complications. The literature is replete with references to this subject, but perhaps I may be permitted to throw a few suggestions into the hopper particularly as they pertain to the otologist's point of view.

Turn now to the treatment of the intracranial complications of ear and sinus infections, reference must be made to the important matter of prevention. This has become doubly significant since the advent of chemotherapy, first, because of the masking effect of the sulfonamide drugs upon the lesions that give rise to intracranial infections and, second, for the reason that these specific chemical substances have greatly altered the prognosis of meningitis and brain abscess. It goes without saying that a surgical mastoiditis or an osteomyelitis of the skull secondary to nasal accessory sinus disease must be recognized and adequately eradicated if we are to give proper attention to our first lines of defense. Heretofore, this was not a difficult task. Years of practical experience recounted the rhinologist with clinical pictures that were more or less typical of surgical lesions and clearly indicated the optimum time for intervention. But the introduction of the sulfonamide drugs has altered the situation somewhat in that we now encounter atypical and protein forms of inflammatory processes within bone which often keep us much in the dark concerning their surgical or nonsurgical character. Under the influence of chemotherapy, particularly its prolonged administration, a mastoid disease may run a bizarre and deceptive course characterized by remissions and a singular absence of the usual signs and symptoms. Its insidious development and perverse growth give rise to osteomyelitic lesions that do not conform to customary patterns and herein lies one of our difficult problems in the diagnosis of surgical mastoiditis in patients who have been treated with the sulfonamide drugs.

Masking, perhaps, is the word that expresses it best. It refers categorically to otological parlance to an infectious process in the mastoid bone that proceeds to its terminal stages with concealed identity. It is this quality of disguise or concealment that makes it a much feared lesion and a serious menace to its neighboring structures.

Turn now to the second influence of chemotherapy to which reference has already been made, it is a matter of verity that the sulfonamide drugs have greatly reduced the mortality of the intracranial complications of ear and sinus infections. Before the discovery of toxic chemical substances

It is highly probable that sulfadiazine will replace the other sulfonamide drugs in otological practice. It is a specific toxic substance for the *Streptococcus viridans*, *Streptococcus hemolyticus*, *pneumococcus* (II types) *meningococcus*, and Friedländer's bacillus. While sulfathiazole is believed to be somewhat superior for staphylococcus infections, there is good scientific evidence that sulfadiazine also has a specific effect upon this organism. It is true that we frequently find a mixed infection in the ear and sinuses with the staphylococcus in great numbers but I am inclined to believe that this organism is usually a "hanger on." The germ that puts in its first appearance, the one that is isolated with the inception of the disease and can usually be found in pure culture in the early stages is probably the real offender and the one upon which the attack should be made.

In addition to its specific effect upon all of the organisms listed above including the staphylococcus, sulfadiazine is less toxic than its related agents. It is much less likely to produce a dermatitis, fever, vomiting, anemia, a peripheral neuritis, psychosis, acidosis, or a hepatitis than either sulfanilamide, sulfathiazole or sulfapyridine. It may therefore be given with little risk in the home provided the patient is seen daily by the physician who will inquire into his state of health and make at least a cursory examination for the common clinical manifestations of a toxic reaction.

It is exceedingly important to commence chemotherapy at the earliest moment in the course of infection and to strike with heavy initial doses. An early knockout is the objective and to this end sulfadiazine is given intravenously in severe infections. The drug is absorbed rather slowly from the gastrointestinal tract and several precious hours may be lost if given by mouth. The initial dose should be 0.1 to 0.15 grams per kilogram of body weight of a 5 per cent solution in freshly distilled water (7 to 0.5 grams for 150 pound man). The preparation should not be autoclaved or boiled. For maintenance dosage by the intravenous route 0.05 grams per kilogram (5 to 7 grams for 150 pound man) is recommended and should be ad-

ministered every 12 to 16 hours. If oral administration is utilized for a maintenance dose 1.0 gram should be given every 4 hours. The blood level should be kept at 10 to 15 milligrams per cent.

Even when large doses of sulfadiazine are given intravenously a proportionately small quantity of it is found in the cerebral spinal fluid. This is in direct contrast to sulfanilamide which is rapidly taken into the spinal fluid and found there in rather high concentration. This observation has led to the supposition that sulfadiazine is less desirable than sulfanilamide in the treatment of meningitis. However it must be borne in mind that in meningitis we are not treating the spinal fluid. We are treating the meninges and experience with sulfadiazine although still meager is promising enough to indicate that it will probably replace its allied preparations in the treatment of intracranial complications of otitis and sinusitis.

CONCLUSIONS

1. While the hematogenous spread of infection from the ear and sinuses to the intracranial structures does occur particularly in the sinusitis of the swimmer, the usual method is by continuity and contiguity of tissue, when the primary lesion has reached the subacute or chronic stages.

A dictum to which we sedulously adhere is, avoid bone work in the presence of a green infection. It is admitted, however, that the exigencies of the disease make surgical intervention imperative in some cases. It may be necessary to sacrifice bone early in the acute process in order to find and drain brain abscess.

3. Meningitis and brain abscess are occasionally chargeable to an intracranial yet extradural infection which spreads in the form of a confluent or patchy exudate over the surface of the dura beneath the inner table of the skull.

4. Treatment calls for the eradication of the primary focus of infection by surgical means and adequate doses of the sulfonamide drugs. Recent experience would seem to indicate that sulfadiazine gives promise of supplanting its allied preparations in the field of otolaryngology.

SURGICAL ANATOMY OF THE EYE

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UNDERSTANDING the anatomy of the eye is essential to any ophthalmic surgeon in performing the various surgical procedures on the globe. It familiarizes him with normal relationships, thereby giving confidence when corrective operations are undertaken in complicated cases. A knowledge of anatomy also includes an understanding of the variations from the normal and the effect these variations play on the functioning of the part. This aids the surgeon when he encounters anomalous relationships.

For instance, it is known that the rectus muscles are covered by fascial sheaths continuous with Tenon's capsule. The connection between the muscle fibers and the sheath is especially strong at the point where the two fuse. Because of this, the muscles retain their attachment to the capsule and do not retract extensively after tenotomy or enucleation of the globe. It is this anatomical arrangement which permits us to obtain some movement of the prosthesis after enucleation and implantation of a foreign substance within Tenon's capsule.

A rather uncommon, but troublesome, complication following enucleation with implantation is a tendency for the implant to migrate in the orbit as if extruded from Tenon's space. This complication may be accounted for on an anatomical basis. If we recall that Tenon's capsule and the conjunctiva are fused with the sclera for a distance of 1 to 2 millimeters about the limbus, and that the cornea has a diameter between 11 and 12 millimeters, we realize that about 16 millimeters of the circumference of Tenon's space has been lost in doing an enucleation and thus the insertion of a glass or metal ball the diameter of the normal eye made impossible. We are able to compute the exact size of ball which can be inserted into the reduced space of tenon following enucleation by subtracting the lost circumference from the circumference of the eyeball. In an adult we find that an implant of more than 18 millimeters will stretch Tenon's capsule and promote its expulsion. Those surgeons recommending a 20 to 21 millimeter diameter implant are forgetting the

size of Tenon's space after enucleation. Upon severance of the optic nerve, a perforation of the capsule is made posteriorly through which an implant is easily forced if too large a one is inserted. These are minor, but important, features to remember in enucleations in which one not only attempts to get the highest percentage in retention of implant, but also to prevent migration of the implant.

In growing subjects, Tenon's capsule is easily separated from the overlying conjunctiva in the anterior segment of the globe, but in adults they are more or less fused. We rely upon the loose capsular and subconjunctival tissue as the bed for absorption of the aqueous in trephine operations for glaucoma. If the conjunctiva and capsule are separated from one another, as in Elliot's original description of the trephine operation, a rather dense scar tissue replaces the normal loose connective tissue resulting in a thin, localized, honeycombed cicatrix at the site of the trephine opening or in no bleb at all. The incision should be through the conjunctiva and capsule, and the relationship between the two should not be disturbed at any step in the operation. This has recently been emphasized by Benedict.

When iridencleisis for glaucoma is performed, it is important to remember that the conjunctiva and Tenon's capsule are fused to the sclera for a distance of 1 to 2 millimeters about the cornea. The fistulizing opening will be under a heavier and looser cushion with less chance of delayed infection, if no attempt is made to dissect the conjunctiva and capsule from the sclera further limbalward than this point of fusion before the keratome incision is performed, since the overlying tissues closer to the cornea are denser and thinner. The sclera has very few blood vessels, and those present consist of branches of the anterior and posterior ciliaries. These form a network almost entirely confined to the episcleral tissues. This episcleral network is extremely attenuated except in the anterior region near the limbus. A close capillary system is formed here which can be evidenced clinically as ciliary injection in inflammatory conditions. This scarcity of blood supply in the sclera partially accounts for the slow healing of scleral wounds. Most of the reparative process advances from the subconjunctival and uveal tissues.

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This slow healing of the sclera promotes the possibility of expulsion of the glass or metal ball when it is implanted in the sclera as in Mules operation. A variable amount of oozing from the perforating vessels, posteriorly and anteriorly may result in the accumulation of a clot which exerts pressure upon the suture line. Tendency for expulsion of the implant is greatly lessened by using silk mattress sutures for closure of the scleral wound anteriorly together with electro-coagulation of the perforating vessels on the inner surface of the sclera. It is essential for one to choose the size of implant which will permit an easy closure of the sclera without tension. Our experience in this type of treatment of the eyeball, when possible has given a far better cosmetic result than simple enucleation or enucleation with implant in Tenon's capsule. We believe there is no more danger here of sympathetic ophthalmia than in any other form of treatment in this surgical condition. Not all cases, however are suitable for a Mules operation. It is reserved for panophthalmitis, freshly lacerated globes, hydrophthalmos, etc., and should not be used when tumor is suspected, or in chronically inflamed eyes.

The thickness of the sclera varies considerably with age and sex. It is thinner in children and in females. The sclera has a thickness of from 0.3 to 0.5 millimeter behind the insertion of the rectus tendon but grows thicker posteriorly. In recession operations, Jameson's directions for inserting the scleral needle should be followed explicitly. One should also remember that the tendons of the rectus muscles become thicker and denser as they approach the sclera. Therefore, if we cut these tendons as close as possible to the sclera, we will retain the densest portion and be assured that our sutures will not tear out after tying.

The limbus offers many anatomical features of clinical importance. In fact too many to be considered entirely at this time. Schlemm's canal is commonly thought of as a single lumen. However it is seldom a single elongated lumen, but more often consists of two or more lumina lying side by side or over one another in the scleral furrow. Salzmann describes it as resembling a great stream which flows along undivided for a stretch, then becomes divided into several branches, and thus differs in various sections of the eye. Therefore Barkan's operation for glaucoma might fail if the incision did not happen to open the lumen, but instead passed between several branches of the canal.

The filtration angle in hydrophthalmos presents many congenital anomalies, no two being exactly alike. These congenital anomalies possibly ac-

count for the poor results obtained in the various operations most commonly used in other forms of glaucoma. In chronic noninflammatory glaucoma the filtration angle is often blocked by anterior root synechia, thus the iris does not herniate into the wound when the scleral button is removed, and no aqueous is lost. In this instance in order to form a communication with the posterior chamber it is necessary to grasp the iris tissue with fine forceps and excise the iris. Undoubtedly all who have performed many trephine operations, on rare occasions have experienced buttonholing of the conjunctival flap at the limbus. I have found Verhoeff's operation for glaucoma well adapted when this has occurred. The buttonhole incision at the limbus above can be continued on either side to make a short conjunctival flap. The epithelium is denuded from the upper pole of the cornea and a trephine opening is made at the usual position on the limbus. The conjunctival flap is drawn down over both the trephine opening and denuded portion of the cornea and, as in the Van Lindt flap is sutured on either side of the cornea. In this, as in other instances, in which it is desirable to cover a portion of the cornea, the anatomical structure of the conjunctiva is such that it lends itself admirably.

The blood supply of the conjunctiva comes from the superior and inferior tarsal arcades of the eyelids and the anterior ciliary arteries. The superior tarsal arcade at the upper border of the tarsus and between the two portions of the levator tendon gives off perforating branches, which pass through the muscle of Mueller to reach the conjunctiva. Here branches are sent downward over the tarsus and upward as the posterior conjunctival vessels to form a superficial pericorneal plexus, after receiving anastomotic branches from the anterior conjunctival arteries. The anterior ciliary artery comes from the muscle branches of the ophthalmic. Each muscle artery gives off two anterior ciliary arteries with the exception of the external rectus which gives only one. The anterior ciliary arteries, after giving off the anterior conjunctival arteries, pass through the sclera at a point just in front of the muscle insertion to enter the base of the iris and form the major arterial circle. The anterior conjunctival vessels are deep to the conjunctiva and do not move with it. They anastomose with the posterior conjunctival vessels, pass on to form the deep pericorneal plexus in the episcleral tissue, and to send vascular loops into the corneal limbus. In cataract extractions, deep incisions into the limbus cut across many of these vascular loops and can cause troublesome bleeding. To a old this trouble some prefer to

perform corneal sections entirely in the cornea. These limbal vascular anatomical findings are of considerable clinical interest. In conjunctivitis and inflammations of the superficial portions of the cornea, it is the superficial pericorneal plexus which is injected. In addition, these vessels move with the conjunctiva but do not fade when pressure is applied. The deep pericorneal plexus is hyperemic in infections of the iris, ciliary body, and deeper corneal stroma. The deep pericorneal plexus is injected in the form of a ciliary flush and it is noted that this flush disappears on pressure but the vessels do not move with the conjunctiva. In interstitial keratitis the new vessels invading the cornea come from the anterior ciliary arteries as they pass through the sclera to reach the iris and ciliary body.

The central third or optical zone of the cornea is spherical. Toward the periphery, especially on its nasal side, it becomes flattened. This explains, in part, the poor visual results obtained with optical iridectomies since it is often necessary to do them behind the flattened zone of the cornea. The optical effect in reducing vision is similar to that obtained in cornea plana.

Wandering cells, corneal corpuscles, and corneal lamellae make up the *substantia propria* of the cornea. The corneal lamellae are broad bands of fibrils which run the entire length of the cornea and nearly parallel to its surface. The bands of fibrils are in alternate layers which crisscross at approximately 90 degrees. This anatomical arrangement offers a line of cleavage in a plane parallel to the corneal surface for resection of corneal scars.

Many believe, in performing an iridectomy for glaucoma, that freeing the filtration angle is the purpose of the operation and that they are successful only in those cases in which the base of the iris has been freely excised from its attachment to the ciliary body. In order to remove a broad portion of the iris base it is necessary that the corneal section be made properly. Meller advises that a sufficiently peripheral position of the section can be obtained if the knife or keratome enters the sclera $1\frac{1}{2}$ millimeters from the limbus and passes approximately parallel to the plane of the iris. This places the inner portion of the incision very close to the base of the iris and allows it to be excised entirely. When the inner portion of the incision is more centrally placed, the iris base is more likely to be left intact and only that portion of the iris central to the incision is removed. These faulty incisions and the iris base left fastened to the inner margin of the wound are often seen in eyes removed after unsuccessful glaucoma opera-

tions. It is best to pick up the base of the iris, push it away from the angle with the iridectomy forceps, and thus produce an iridodialysis when the incision is known to be faulty or if it is thought desirable to retain the sphincter action if subsequent miotic therapy should be needed. The base of the iris is then excised horizontally producing a large peripheral coloboma, but retaining sphincter action. Because some of the patients might need miotic therapy as an accessory aid in reducing the intraocular tension, I can see no advantage in producing a complete coloboma in either iridectomies or trephines.

The iris has a few interesting anatomical characteristics. One is its absence of hemorrhagic tendency after cutting, and another, its failure to heal following iridectomy. However, when there is inflammatory tissue on its surface or new formed blood vessels of inflammatory origin, we do find a tendency for bleeding and secondary proliferation following the trauma produced by surgery. The blood vessels in this inflammatory membrane are entirely different in character from those of the normal iris. Their walls are much thinner and contain much less contractile element, thereby giving them less hemostatic effect.

In the posterior uvea we find the choriocapillaris supplied by the posterior ciliary arteries. Anterior to the equator the blood comes from the recurrent branches of the long posterior ciliary arteries. The relatively few anastomoses between these two sources have been sited as the cause for circulatory failure of the intermediate zone at the equator in certain cases, that is, in producing the ring scotoma of pigmentary degeneration of the retina. However, ring scotoma in retinitis pigmentosa is at about the 20 to 30 degree meridian, which is in the zone of the posterior ciliary circulation and thus posterior to this junction. Ring scotoma at the equator is seen in luetic disease of the arteries and can thus be used as a differential point in diagnosing these two clinical conditions.

Between the sclera and the choroid is the perichoroidal space, a potential cavity across which the fine lamellae of the superficial layer of the choroid stretch to blend with the lamina fusca of the sclera. This space, which is traversed by the vessels and nerves supplying the choroid, stretches between the scleral spur and the optic scleral foramen. The choroid is easily detached from the sclera during cataract or glaucoma surgery because of the delicate nature of lamellae stretching across it. Torn lamina heals without residual visual loss after absorption of subchoroidal edema fluid. On the other hand, the inner surface of the choroid is very intimately related to the outer lay-

ers of the retina indeed, the basal membrane separating the two structures is partly derived from each, and the pigment epithelium of the retina is very closely associated with this membrane. When the retina is detached, the split occurs between the neural layers of the retina and the retinal epithelium the latter structure remaining behind and adhering to the choroid.

Salzmann finds that the suprachoroides is at length completely lost in the meridional portion of the ciliary muscle. The majority of the lamellae enter the posterior border of the ciliary muscle with the result that the most anterior portion of the suprachoroidal space must be entirely free of suprachoroidal lamellae. Because of the density of the lamina and the absence of the suprachoroides beneath at least the anterior half of the width of the ciliary region, I would suggest that the scleral opening be at least 5 millimeters from the limbus in doing a cyclodialysis for glaucoma. This would connect the channel made to the anterior chamber with the lower suprachoroidal space behind the midpoint of the ciliary muscle.

The anatomy of this area of the globe has another important clinical application when we recall that the ciliary body has a width of about 5 to 6 millimeters (Salzmann) as measured on the inner surface of the sclera or 7 to 8 millimeters as measured on the outer surface of the sclera. Let us recall also, that the corona ciliaris is about 2 millimeters broad, or when measured on the outer surface of the sclera 3 to 3.5 millimeters, and that the orbicularis ciliaris has a width of 4.5 to 5 millimeters on the outer scleral surface. The orbicularis ciliaris of the ciliary body contains a vascular layer much like that of the choroid with which it is continuous. It is not, however so wide and there is no choriocapillaris. This is the least vascular structure or area of the eyeball outside of the cornea. Since the arterial supply to the whole anterior region of the uvea passes through the ciliary muscle, the vessels in the orbicularis ciliaris consist almost entirely of veins which run backward meridionally and parallel to each other to empty into the vena vorticosae. These anatomical considerations seem to point to the orbicularis ciliaris of the ciliary body as the most optimum site of entrance to remove intraocular metallic foreign bodies by the posterior route. There is no danger of detachment of the retina if a hinged scleral trephine button is made just anterior to the ora serrata and the underlying uvea incised meridionally with a cataract knife. This might occur if the opening were made further posteriorly. There is a minimum of hemorrhage since the least vascu-

lar zone of the posterior segment is entered. The postoperative reaction is surprisingly slight. The wound heals readily and without tendency for staphyloma. I can see no reason for fearing sympathetic ophthalmia. This approach has been used with much satisfaction in the University Clinic for over 10 years (1).

By recognizing the structure of the retina it is easy to understand that hemorrhage occurring in the nerve fiber layers are the flame shaped type of hemorrhages. More irregularly spreading or punctate hemorrhages are seen when they occur in the nuclear or plexiform layers. It must be borne in mind that the anatomical structure of even the largest branches of the central retinal artery resembles that of the arterioles in the thinness of their walls and in the absence or slight development of the muscular coat. Those designating the branches of the central artery of the retina in the first and second order as arteries, and the finer divisions, as arterioles, are basing this view upon the marked differences in their clinical manifestations in hypertension, rather than upon differences in anatomical structure. Anatomically there is little if any difference, in the various branches of the central retinal artery.

The functional retina extends to within 7 millimeters of the ora. Structurally the nonfunctional retina is frequently degenerate and thus after the age of 30 it almost constantly shows a varying number of cysts which may in some cases atrophy to such a degree that vitreous is allowed to extend through it and cause retinal separation. Once the retina is separated, its full functions are never restored following reattachment. This is especially true when the macular area is detached in that central vision seldom, if ever is restored to its former acuity. Most patients complain of metamorphopsia and marked disturbances in reading vision.

The peripheral retina to the extent of about 4 millimeters is seldom visible with the ophthalmoscope even with a widely dilated pupil. This must be remembered in order to determine the distance of retinal tears from the ora in retinal separation. In less widely dilated pupils, of course, not even this much of the periphery is visible. Since the ora is considered to be 8 millimeters from the limbus as measured on the sclera, the anterior limits of the usual ophthalmoscopic field are approximately 1 millimeter from the limbus. It is convenient to remember that the optic nerve head is 4 1/4 millimeters in diameter and to estimate the distance of the retinal tears from the ora in disc diameters. With these measurements available at the time of operation, the

position of the retinal tears may be projected to the scleral surface with fair accuracy

The central retinal artery and vein enter the optic nerve 5 to 15 millimeters behind the eyeball on its lower and mesial aspect. The artery usually goes directly through the subarachnoid space to reach the center of the optic nerve, where it turns at right angles to send a recurrent branch backward, while the central retinal artery goes toward the optic disc. The vein enters the subarachnoid space and courses anteriorly a short distance through it before turning at right angles to reach the center of the optic nerve, where it in turn sends its recurrent branch, and then goes toward the optic disc as the central retinal vein. Thus, it is seen that the veins can be affected by any rise in pressure to which the fluid in the subarachnoid space is subjected, and papilledema may result, as in the case of increased intracranial pressure.

Fincham has demonstrated that the thickness of the lens capsule varies in different portions, and gradually thickens with increasing years. The thickest portion of the capsule is found to be limited to a zone running around concentrically with the equator and just central to the insertion of the zonular fibers on both the anterior and posterior surface of the lens. The fact that the zonular fibers weaken with age and the lens capsule thickens with age accounts for the greater ease of intracapsular extractions in elderly people.

As the anterior ciliary arteries and veins pass through the scleral emissaria anterior to the muscle attachments, they are sometimes accompanied by aberrant intrascleral nerve loops from the long ciliary nerves in the perichoroidal space. On occasions, because these nerve loops are so pigmented, they give the appearance of subconjunctival metallic foreign bodies and unless the patient is well anesthetized excruciating pain is experienced upon attempting to remove them.

During external ethmoid operations it is of importance to remember the length of the optic nerve. The average length of the optic nerve is 25 millimeters between the globe and the optic foramen, while the average distance between the posterior pole of the eye and the optic foramen is 18 millimeters. This allows a possible forward displacement of the globe 7 millimeters before the nerve is put on a tension that might produce optic atrophy. In order to obtain better exposure during external ethmoid operations, I have seen a few instances in which too much traction on the globe has resulted in immediate and complete loss of vision.

SUMMARY

A few anatomical features of the eyeball have been presented in the hope of rationalizing various surgical procedures, and only with such knowledge is the surgeon capable of carrying out operative technique with the greatest finesse and with the least possible complications. A thorough understanding of the structures involved in a surgical problem will greatly influence the choice of method used, if several methods of approach are possible. No new operative methods have been presented, but a review of a few of the known anatomical features has been given in an attempt to draw attention to certain pitfalls in present surgical methods used on the eye which might be avoided through a better knowledge of anatomy.

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ers of the retina indeed, the basal membrane separating the two structures is partly derived from each, and the pigment epithelium of the retina is very closely associated with this membrane. When the retina is detached the split occurs between the neural layers of the retina and the retinal epithelium the latter structure remaining behind and adhering to the choroid.

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FRALICK SURGICAL ANATOMY OF THE EYE

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RETROBULBAR NEURITIS IN RELATION TO SINUS DISEASE

JAMES B. COSTEN M.D. F.A.C.S., St. Louis, Missouri

NO subject in the entire field of otolaryngology has been capable of exciting such perennial interest and controversy as the relationship of retrobulbar neuritis to sinus disease. Many such cases had been reported as relieved by opening of the nasal sinuses but close anatomical relationship was revealed in the studies of Onodi in 1908. He demonstrated how frequently the optic nerve passes along the upper and outer wall of the sphenoid and posterior ethmoid cells, covered only by a thin bone or membrane. To remove the effects of direct absorption of pus or the pressure from thickened membranes seemed merely to require resection of this posterior group of sinuses.

Hajak, Sluder, Sauer, Loeb and others of that era reported many successful cases in which the blindness was relieved after such surgery. The recognition of multiple sclerosis as the commonest cause of retrobulbar neuritis discounted many of the early successful cases and incited further interest in the etiology of the disease.

It was recognized as a lesion of the papillomacular bundle with enlargement of the blind spot and central scotoma without visible change in the appearance of the eye grounds. Gracie ascribed this to the involvement of the central vein of Vossius, secondary to the involvement of the perosteal or dural veins adjacent to the diseased sinuses.

L. White (20) made most important studies, beginning in 1913, on the relationship of the diameter of the optic canal to the prognosis, finding that 50 per cent of patients with optic nerve involvement having 4 millimeter canal measurements were unimproved, regardless of the type of treatment. He showed that extensive pneumatization of the sphenoid next to the canal is usually associated with a smaller caliber canal and thinning of its bone. He urged the search for an elimination of all distant foci (8) becoming more and more conservative with regard to the surgical drainage of posterior sinuses.

As the preponderance of multiple sclerosis gave it first place in etiology of this type of optic neur-

itis, toxic effects from chemicals, alcohol, and tobacco from diabetes, nephritis, and virus diseases became recognized as next in frequency, raising the figures of toxic absorption from the sinuses to the bottom of the list. Authentic reports revealing sinus disease clearly as the cause had been made by Oliver and Crowe in 1917 and Peter in 1918. Ellett in 1929 reported cases of prompt recovery of vision after drainage of sinuses as well as after removal of teeth. He emphasized the need of careful analysis of the case before selecting treatment. Benedict and Lillie in similar reports found the incidence of proved sinus infection so low in the study of large series of retrobulbar neuritis that they both considered its importance negligible. Campbell, after a comprehensive review of numerous authors giving discouraging opinions, conceded that there is in a small percentage of cases an actual indication for surgical drainage of the sinuses in retrobulbar neuritis. The study of Kennedy in 1936, definitely established allergy as an important cause of retrobulbar neuritis to be considered in every case until any possible allergic factor has been removed from context.

Early stages of visual disturbance in retrobulbar neuritis may be only vague subjective symptoms such as blurring which clears up rapidly. It is unlikely that many in this stage are examined. To proceed with diagnosis, multiple sclerosis must be ruled out by its numerous neurological signs and differentiated from syphilis by the use of both blood and spinal fluid serological tests. Any preceding acute febrile disease or chronic exposure to chemicals, nicotine, or alcohol is sought in the history. Foci such as diseased tonsils and teeth are carefully examined and elaborate study of the paranasal sinuses is made. Besides routine x-ray positions, lipiodol plates, made by puncture of maxillaries and by Proetz (16) displacements into sphenoids, are of great value. Laminograms made at 5, 6 and 7 centimeter levels in the coronal plane of the head, recently described by Coon, Dean, and Moore, aid greatly in the estimation of density in the posterior group of sinuses, in this district superimposed cells can be truly analyzed by this method only.

In 1939 a personal series of 13 cases (5) as presented before the Southern Medical Association,

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Presented before the Clinical Congress of the American College of Surgeons, Boston, November 3-7, 1941.

to Barnes Hospital in 1 of which a diagnosis of retrobulbar neuritis was made. The principal contributing factors noted in the 27 cases of retrobulbar neuritis were remote foci in 6 cases, alcohol in 3 cases, brain tumor in 2 cases, sinus disease in 8 cases, systemic disease in 3 cases, complicating allergy in 2. Of the 27 patients with a diagnosis of retrobulbar neuritis, the condition of 8 was improved by sphenoidectomy, 1 after 2 years, 6 were improved by typhoid and fever therapy, 2 made a spontaneous recovery with no treatment. One is reviewed in detail with the permission of Doctors Cone and Votaw. It is of particular interest because there is an unproved allergy in the history, prompt recovery of the patient after surgery of diseased sinuses and a follow-up for 2½ years with no further visual disturbance.

CASE 6 W W R, aged 22 years, a white female, entered Barnes Hospital April 7, 1939, with failing vision of 3 weeks which had followed a left frontal headache with no preceding throat or nose obstruction. She gave a history of hives and angioneurotic edema in January, 1939 after eating shrimp, but no likely causative agent was taken before this attack. Examination by Dr. Lawrence Post showed vision 20/60 in the left eye with an eccentric scotoma. Nose and throat examination was entirely negative except for delayed emptying of the left posterior noid. Laminagrams had shown blurring of the left sphenoid section of the left sphenoid and ethmoid cells was done with marked improvement of vision in the left eye in 3 days. Section of tissues from the sinuses showed marked inflammatory change. The vision on May 10, 1939, in the left eye was 20/25-2.

Whatever is done for the relief of retrobulbar neuritis or for extensive acute retinal lesions, in the way of sinus surgery or removal of foci, should be promptly carried out, damage to the optic nerve being rapid and commonly followed by permanent residual atrophy. The opportunity to demonstrate improvement after surgery is limited because the cases showing indications are few in number, and the surgery is done concurrently with all forms of general therapy. When used there are various theories regarding the value of surgery of the sinuses.

- 1 Drainage of infectious material away from direct contact with the optic nerve
- 2 Removal of a negative pressure effect within the sinuses which produce an emigration of toxins and bacteria to the tissues about the optic nerve (White, 20)
- 3 Decompression of the nerve by free incision of blood and lymphatic vessels when engorged tissues are removed (Proetz, 17)
- 4 Production of hyperemia, restoring blood supply to the nerve, anemic from swelling within

the bony canal or by thrombosis of small vessels supplying them. Benedict and Lilhe believe that the same thing may be accomplished by the use of stimulating chemicals within the nose. A most elaborate survey by Duggan, 1941, takes a strong stand against removal of foci except for the sake of removal as a toxic source—and not that such removal would influence an angiospastic lesion to which he thinks retrobulbar neuritis belongs, he considers it a localized tissue anoxia, a histamine effect, and a "vasodilating therapy directed toward these pathological changes is both logical and effective—that nasal sinus surgery is nonspecific in mode of action—and that improvement of vision is more rapid and more marked (with vasodilator treatment) than when other types or no therapy at all is used."

CONCLUSION

Even though the question should remain open because of so many qualifying factors, surgery of any diseased sinuses seems to be indicated when the condition occurs in its rare association with retrobulbar neuritis. The presence of allergy increases the indication for surgery according to our experience. Study of the records certainly confirms the stated importance of removal of foci distant from the optic nerve, such as teeth and tonsils. The use of laminagrams is a valuable addition to the x-ray study of posterior sinus disease.

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TABLE I—CASES OF RETROBULBAR NEURITIS (27) ADMITTED TO BARNES HOSPITAL FROM 1929 TO 1939

Age	Sex	Eyes involved	Concurrent disease	General therapy	Local therapy	Course
22	M	Both	Multiple sclerosis	Not treated		Not improved
28	F	Both			Spherothamidoctomy bilateral	Improved
38	M	Both	Alcohol abscesses	Not treated		Not improved
	M	Both		Intravenous typhoid		Improved
47	M (Col.)	Both	Diabetes	Insulin		Improved
57	M	Both	Alcohol and tuberculous amblyopia	Intravenous typhoid	Tamoxifony	Improved
43	M	Both	Alcohol arteriosclerosis	Lamb alcohol		Improved
62	M	Both	Nephrosclerosis & meningitis basilar			Not treated
56	M	Both			Tamoxifony	Improved
54	F	L			Spherothamidoctomy bilateral	Improved
48	M	Both	Prostatitis chronic	Intravenous typhoid	Tamoxifony	Improved
44	M	Both	Central nervous system syphilis	Fever therapy hyperthermia		Not improved
53	F	Both	Hypothyroidism		Diphtheria antitoxin	Improved
60	M	Both	Hysteria?			Not treated
51	M	Both			Tamoxifony	Improvement
56	M (Col.)	Both			Spherothamidoctomy bilateral Astrum windows	Improved
53	M	R.	Spherothamidoctomy		Spherothamidoctomy right	Improved
61	M	Both	Cystitis of lower right	Not treated		Not improved
61	M	Both	Brain tumor, adenoma of pituitary	Craniotomy	Tamoxifony	Not improved
52	F	Both	Brain tumor choriocarcinoma	Choriocarcinoma chemotherapy (A)		Improved
56	M	Both		Intravenous typhoid	Spherothamidoctomy bilateral Tamoxifony	Improved 75% constriction, dark
50	F	L		Intravenous typhoid		Improved
54	F (Col.)	L		Intravenous typhoid	Cases not found	Improved
64	M	Both	Alcohol arteriosclerosis Hypertension	Vitamin therapy		Improved
45	F	Both	Psychoneurosis		Spherothamidoctomy bilateral	Improved
50	F	Both	Allergy		Spherothamidoctomy bilateral	Improved
52	F	L	Allergy, lewis		Spherothamidoctomy, left	Improved

is a variety of retinal lesions, all seen during an acute stage and all responding more or less promptly to surgical drainage of sinuses, and removal of tonsils. Cases 1 and 5 had definite allergy the latter patient becoming very sensitive to drugs used in the eye. Although she had responded to fever therapy with remission of symptoms, the longest period of improvement began at once after clearing out the maxillary sinuses and she is more comfortable now than at any period of her complicated eye history. Case 1 belongs to

the group classified as lactation amblyopia (Imachi and Maruoka, and Sautter) for which Sautter's treatment was salicylate sweats, high doses of vitamin B₁₂ and calcium preparations.

In review of all patients with optic neuritis admitted to Barnes Hospital in the past 10 years—85 in number not including records of out patient dispensary of Washington University—it is noted that in 27 a diagnosis of retrobulbar neuritis was made (Table I). During the same period there were 195 cases of multiple sclerosis admitted

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MANAGEMENT OF OPHTHALMOLOGICAL SURGICAL COMPLICATIONS

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In its broadest sense surgical complications imply not only the complications of the actual surgical procedure, but also the undesirable and unlooked for reactions to surgery, on remote parts of the body. These can be divided roughly into three large groups. The first group comprises conditions in which surgery is attended by grave risks, the second, cases in which the eyes themselves have given evidence of intolerance to any surgery. The third group is made up of cases in which one would naturally expect a good result but complications arise through fortuitous circumstances such as the patient falling out of bed or becoming delirious and pulling off the bandages and injuring the eye.

First let us consider that group of cases in which life expectancy is short, i.e., malignancy or advanced senility or great physical depression. Only the most necessary of operations should be done. Sometimes however even in advanced senility one obtains very favorable results. I remember operating on a patient at the clinic who was 96 years old and had a tumor of the iris. It seemed to be well localized but was growing. He came of a long lived family, his father being 100 years of age at the time of death and his mother well along in years. He himself was in very good health considering his years. He recovered from the iridectomy and apparently there were no metastases. A year and a half later I removed the lens of the eye because the vision had deteriorated to less than 20/300. He recovered in the usual time without complications with vision of 20/40. There was very slight macular degeneration. He read large printed matter for several years. He lived to the age of 103 years.

In systemic diseases such as advanced tuberculosis great care should be taken not to do unnecessary surgery, particularly such surgery as will require the patient to lie quietly on his back for a day or two. In diabetes one does not worry as much as one used to. Our practice is to put the patient in the hospital for several days or a week before operation—sometimes longer—so that the diabetic service will be able to control the situ-

ation. We do not operate until that service tells us to go ahead. In acute infections such as diphtheria, scarlet fever or acute colds one must be exceptionally careful. All but the most urgent surgery should be postponed. I recall a little Chinese boy who was brought in with a bad laceration of the eye. He had fallen on a milk bottle. The cornea had to be sewed up immediately although he had a fever of 101 degrees and a bronchitis that was very evident. In this case intravenous anesthesia was given, the eye was sewed up, the conjunctival flap was brought over and the patient then put on the medical service. There were no serious complications.

Infections around the teeth and gums, to my mind, constitute contraindications for any but immediate surgery. The mouth should be cleaned up first and any pockets of pus or infected roots should be treated or the teeth removed. We are more apt to see these patients in the clinic than in private practice and therefore are apt to overlook the obvious.

Let us next take that group of cases in which we have learned to expect only grief for instance an acute inflammation in the sympathizing eye of sympathetic ophthalmia.

CASE REPORT

Mr. Joon, No. C 3553, 74 years of age, was brought to me with a history that nearsightedness had begun 19 months before. A diagnosis of cataract had been made and the left eye was operated upon in December 1935, about 8 months before I saw him. Apparently there was post-operative prolapse of the iris. He left the hospital 5 days after the operation and the eye began to pain him very greatly. His doctor told him he had an infection and sent him to dentist, he found good many of his teeth in bad condition. Nearly all of these were extracted during the succeeding several months but there was no improvement in his eyesight. At times there was very great pain which began to affect the right eye about 3 months before I saw him, that is, in May. This right eye had been perfectly normal before the operation according to his story and he had been advised that no operation would be necessary upon that eye.

I found his left vision was 0, the tension - 3. The eye was markedly inflamed and shrunken. The cornea was milky and wrinkled and the eyeball was conspicuously tender. The right eye was not particularly inflamed, the vision counting fingers at 6 feet in dim light. The pupil was undilated and vertically oval, about 3.5 by 4 millimeters. There was gray reflex in the pupil. The anterior chamber was of fair depth. There were few precipitates

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on the lower portion of the cornea and several pupillary synechiae. Considerable pigment was present on the anterior capsule and there was clouding of the cortex. No cycloplegic or mydriatic had been used in this eye according to the patient's statement.

After atropine was used in the right eye, 3 rather firm adhesions were found and there was a marked opacity on the posterior pole of the lens so that it interfered considerably with the view of the fundus. A faint view of one artery only was seen in the fundus.

In order to relieve him of pain the left eye was enucleated, and the routine medical treatment for sympathetic uveitis of the right eye instituted, salicylates, typhoid vaccine intravenously, local heat and cycloplegia. The iritis rather promptly subsided, but it would recur from time to time, lasting for a few days. The tension of this eye was within normal limits for some weeks but it gradually increased and neither cycloplegics nor miotics helped. He was carried along with a tension in the 30's for about 6 months, when the tension rose to 60 millimeters of mercury, at which time he was hospitalized and a paracentesis done. Following this the eye remained quiet for a month, when suddenly there developed considerable pain in the eye and I found a spontaneous rupture of the anterior capsule of the lens, just below the center. Cortex was found in the anterior chamber. The tension was considerably increased but the eye was too tender for us to use the tonometer.

In consultation with both Dr. Gradle and with Dr. Brawley it was decided to attempt an immediate removal of the lens and the capsule if possible. The lens could not be removed; the capsule naturally because the capsule had already ruptured. After VanLint akinesia and a retrobulbar anesthesia of the ciliary ganglion and 1 per cent cocaine subconjunctivally was used to assure complete anesthesia, I dissected a conjunctival flap down from about 4 millimeters from the limbus and placed the sutures before making a corneal section. The corneal section was then done, a complete root iridectomy was obtained, the nucleus and cortex were expressed and the chamber irrigated without complications. It was impossible to remove much of the anterior capsule.

At first dressing the pupil was found filled with an exudate and the iris was quite thick. The pupil remained fairly large but the anterior chamber did not form. Connected with the pupillary exudate was a yellowish white thick mass which lay on a portion of the iris and in the colobomatous area and there was a distinct tumefaction of the iris at 11 o'clock. He was markedly sensitive to atropine and scopolamine so duboisine was used. The tumefaction in the iris gradually subsided and the cornea seemed to become more normal. As the anterior chamber reformed it was filled with exudate so that there was no aqueous interval seen with the slit lamp beam. Two months after the operation there were minute hemorrhages present on the lens capsule and iris. Later the cornea became quite vascularized, the projection was very poor, the tension became minus and the sclera began to shrink. The vision of course was 0.

I cite this case for several reasons. In the first place, the time to begin to handle surgical complications is *before surgery is attempted*. This man's teeth did not suddenly become worse after the cataract operation was done. The teeth should have been put in order before the first cataract operation was done. One should also anticipate possible complications of a prostatic nature or a gall bladder nature or a bowel nature.

My uncle was operated upon unsuccessfully in Florida for cataract because the doctor had not recognized a habitual cough that he could not control. This cough racked him at least twice an hour during his waking hours. Naturally he had a prolapse of the iris and a detachment of the retina. It is easier to manage these surgical complications before we attempt surgery rather than afterward.

Another reason I have cited this case in such length is because of the short period of hospitalization following the cataract extraction. The operation was done on December 3, and he left the hospital on December 8. It is true that cataracts used to be done in the doctor's office and the patient allowed to go home the same day, possibly 8 or 10 miles into the country in a farm wagon, but you would not wish to have yourself or your relatives so treated. One of the most careful surgeons in the United States keeps his patients flat on their backs for several days, occasionally 2 weeks, after the operation and practically never lets them leave the hospital under 2 weeks. Some years ago I was impressed by the action of a general surgeon who removed my wife's gall bladder. It was a beautiful operation, clean anatomical dissection, clean anatomical removal. I marvelled that he did not look at the wound for 10 days. He was sure of his surgery. He was sure of his technique. I wonder how many of us can keep our hands off an eye that has been operated upon for cataract for 3 or 4 or 5 days after operation.

Another reason I quoted this history was the fact that the patient's right vision was normal, so he said, and he quoted the doctor as saying that no operation would have to be done on the right eye. Seldom do we need to operate for cataract when the vision of the other eye is good. Very occasionally we will find an overripe cataract or a cataract beginning to become overripe in one eye and no opacity or only an immature cataract in the other eye, the vision in the second eye being nearly normal.

Still another reason is that the doctor apparently lost interest in the case at a most critical time merely turning him over to the dentist who was in a distant city. Also, he did not recognize over a period of 2 months, the beginning signs of sympathetic ophthalmia or he would not have rested until the exciting eye had been removed.

I cannot emphasize too strongly. First, the most important thing in the management of complications is to *avoid having them* by careful preoperative study of the case and by refusing to operate upon patients unless there is definite

indication therefor. Second, consultation is always in order. The patients may protest that they think highly of us but they know that none of us is all wise and seldom do we find a patient who will not welcome consultation. The patient must have thorough confidence in the surgeon and the surgeon in himself.

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On our service at the Illinois Eye and Ear Infirmary we have found that since our technique has been slightly changed prolapses are very much fewer than they used to be. On our service there are two first assistants who alternate in the operating room, changing off every 3 months. One is a staunch advocate of the Verhoeff radiating limbal suture with conjunctival cowl. The other uses parallel corneoscleral sutures with conjunctival cowl. Otherwise their techniques are quite similar and include culture from the conjunctiva taken 48 hours before the operation and at the operation, akinesia and ciliary ganglion anesthesia, iridectomy (peripheral or complete), careful extraction, careful postoperative toilet and a preliminary canthotomy if the patient is unco-operative or the eyeball is rather prominent. Their desire is to produce nonleaking close approximation of the wound. Dr. Leech examines his patients after 48 hours, Dr. Nethercut and I, after 96 hours. In case pain or suggestive fever occurs before the time for the regular dressing naturally our routine calls for immediate investigation of its cause. The first dressing is the most important as at that time careful handling will avoid prolapses that careless handling would produce. The careless removal of the dressings or raising of the upper lid with the thumb placed

over the supraorbital notch has caused more than one prolapse. The thumb should be placed temporal to the supraorbital notch and the lid should be very gently raised.

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Larger prolapses and those not covered with conjunctiva have to be handled surgically. It is my opinion that as a rule we do not spend enough time planning our course of action, and certainly not enough time to get complete anesthesia when operation is decided upon. Also we are too anxious to get through with the operation, to cover up the eye to hide our errors of technique with a bandage. One must be exceedingly delicate as the tissues are very thin and undue haste or pressure will cause disastrous loss of vitreous. The part must be thoroughly anesthetized by retrobulbar and subconjunctival injection as well as topical application so that there will be absolutely no feeling. This anesthesia is decidedly more difficult than at the time of the first operation. One must remember also that unless the eyeball is soft before it is opened, as soon as the prolapsed iris is cut, vitreous will present. Therefore in the retrobulbar injections, enough adrenalin must be used with the anesthetic to cause a tension of -1 to the finger within 10 minutes. We wait until that softening occurs before opening the wound.

Some sort of a conjunctival flap must be prepared before the prolapse is excised. This can be a sliding flap or a simple cowl. Sutures must be placed in the corneal and/or the scleral tissues. If one bears in mind the histological relationship in a case of prolapse he will better understand

how to handle the situation. A prolapse means that there is very little tissue between the contents of the eye and the outside world. At the edge of the prolapse the cornea and/or sclera are shelved to almost infinitesimal thinness. If the prolapse is large how can one expect to provide protection with only a conjunctival flap? It is essential to have the edges of cornea or sclera meet in such a way that they will grow together and be firm enough to withstand the postoperative intraocular tension. This may be aided by doing a cyclodialysis immediately after the prolapse is excised. Canthotomy will relieve postoperative pressure from without; this is imperative in the so-called "squeezeers."

The actual excision is to my mind best preceded by a very light cautery, either chemical or thermal, of the epithelial structures that cover the prolapse and the nearby tissues, that is, for *at least 2 millimeters* beyond the prolapse. When the eyeball is thoroughly softened and after the conjunctival flap is prepared, one should carefully dissect down until the iris is reached at the root on both ends and on the scleral side of the prolapse. The iris is then grasped and an attempt made to free it very delicately from the *corneal* adhesions. This can usually be done with the fine forceps but occasionally a spatula is necessary. The prolapsed iris should be pulled out away from the adhesions to both distal and proximal edges and carefully excised so that the part remaining will retract. The corneoscleral edge is then very carefully prepared with the scissors in such a way that the drawing up of the sutures will cause an exact approximation of the two edges. Interrupted fine silk sutures threaded on small corneal needles are placed perpendicular to the wound so as to hold the edges together and make it watertight; they penetrate only the anterior layers of stroma. The sutures are then drawn up to demonstrate this and before being tied, their ends are passed through the conjunctival cowl. The sutures should be tied snugly but not so tightly as to invert or evert the edges. When they are tied we therefore have accurate approximation of an appreciable thickness of cornea and an appreciable thickness of sclera from the anterior surface of which all epithelium has been removed for at least 2 millimeters. The raw surface of the conjunctiva therefore has a chance to send down into these tissues new-formed blood vessels. Such an eye should be immediately treated with atropine and bichloride ointment and both eyes bandaged. It should not be re-examined for *at least 4 days*. Our recurrences are due to meddlesome inquisitiveness which should not be tolerated.

If we do our surgery well, we do not have to be meddlesome. If we do not do our surgery well, we should quit doing surgery. Prolapses sometimes occur in the best of hands but too many of them indicate poor surgery.

One of the most embarrassing complications which we encounter is an inability to extract the lens before loss of vitreous has taken place. This may be due to an improper corneal section. Recently one of the residents who had had some experience, inserted the cataract knife back of the iris. The anterior chamber in this case was particularly shallow and a corneal section should not have been attempted in the usual way. The knife was withdrawn and the section was completed by the attending surgeon with the aid of scissors. Fortunately the Verhoeff sutures had been previously placed and were ready to be tied before the attempted removal of the lens. When the iridectomy was done vitreous presented. The speculum was removed and the eye was closed for 5 minutes. The upper lid was raised with the suture which had previously been placed in it and a DeMarr retractor was inserted. The vitreous had replaced itself, the blood was washed out of the anterior chamber and on attempting to grasp the capsule with the forceps, again vitreous presented. To go after the lens in the usual way would have invited certain disaster. Consequently a thin probe with a very smooth knob at its end was used to break a few zonular fibers at a time. In order to do this the corneal lip had to be raised very gently. The fact that vitreous presented in the wound meant that some of the zonular fibers had already ruptured. Therefore the first to be ruptured intentionally were the lower ones, then those on each side, a few at a time, until nearly all of them were ruptured, after which the lens was easily removed with the loop. The Verhoeff sutures were pulled up and before being tied, the prolapsed vitreous was very carefully excised. (One must be cautious in this maneuver as the sutures can be cut so easily.) The sutures were then tied, and with a spatula, the iris was freed from the wound.

The removal of a lens freely floating in the vitreous presents many difficulties. Particularly is this so when it does not disappear into the vitreous until after the section has been made. This can best be handled by the use of a focussed fluorescent light, or by locating the lens with the ophthalmoscope, using a fluorescent light. Great care must be taken not to injure the retina as a hole is very often produced and detachment of the retina invariably results. It is considered better surgery to leave it alone unless it can be floated

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over the supraorbital notch has caused more than one prolapse. The thumb should be placed temporal to the supraorbital notch and the lid should be very gently raised.

But once a prolapse occurs, it should be recognized and notations of its first appearance made upon the record. I am not inclined to touch it for nearly a week unless it occurs within 48 hours as I wish the wound to be as firmly healed in the rest of its extent, as is possible. At the end of week, depending upon its size and whether or not it is covered with conjunctiva, the treatment begins. If it is a small prolapse and covered entirely with conjunctiva, after anesthetizing with pontocaine we touch the prolapse with a very small applicator dipped in trichloroacetic acid. This treatment is repeated daily. It is important immediately before this treatment, to dry the area to be treated. The trichloroacetic acid is a saturated solution. A dry cotton-tipped applicator should then be applied so that the trichloroacetic acid will not touch other parts of the eye. This treatment is repeated daily for a week, then 3 times a week for 3 weeks. It is remarkable how many of these prolapses will flatten out under this treatment without further complication.

Larger prolapses and those not covered with conjunctiva have to be handled surgically. It is my opinion that as a rule we do not spend enough time planning our course of action, and certainly not enough time to get complete anesthesia when operation is decided upon. Also we are too anxious to get through with the operation, to cover up the eye to hide our errors of technique with a bandage. One must be exceedingly delicate as the tissues are very thin and undue haste or pressure will cause disastrous loss of vitreous. The part must be thoroughly anesthetized by retrobulbar and subconjunctival injection as well as topical application so that there will be absolutely no feeling. This anesthetization is decidedly more difficult than at the time of the first operation. One must remember also that unless the eyeball is soft before it is opened, as soon as the prolapsed iris is cut, vitreous will present. Therefore in the retrobulbar injections, enough adrenalin must be used with the anesthetic to cause a tension of -1 to the fingers within 10 minutes. We wait until that softening occurs before opening the wound.

Some sort of a conjunctival flap must be prepared before the prolapse is excised. This can be a sliding flap or a simple cowl. Sutures must be placed in the corneal and/or the scleral tissues. If one bears in mind the histological relationship in a case of prolapse he will better understand

how to handle the situation. A prolapse means that there is very little tissue between the contents of the eye and the outside world. At the edge of the prolapse the cornea and/or sclera are shelved to almost infinitesimal thinness. If the prolapse is large how can one expect to provide protection with only a conjunctival flap? It is essential to have the edges of cornea or sclera meet in such a way that they will grow together and be firm enough to withstand the postoperative intraocular tension. This may be aided by doing a cyclodialysis immediately after the prolapse is excised. Canthotomy will relieve postoperative pressure from without, this is imperative in the so-called "squeezers."

The actual excision is to my mind best preceded by a very light cautery, either chemical or thermal, of the epithelial structures that cover the prolapse and the nearby tissues, that is, for *at least* 2 millimeters beyond the prolapse. When the eyeball is thoroughly softened and after the conjunctival flap is prepared, one should carefully dissect down until the iris is reached at the root on both ends and on the scleral side of the prolapse. The iris is then grasped and an attempt made to free it very delicately from the *corneal* adhesions. This can usually be done with the fine forceps but occasionally a spatula is necessary. The prolapsed iris should be pulled out away from the adhesions to both distal and proximal edges and carefully excised so that the part remaining will retract. The corneoscleral edge is then very carefully prepared with the scissors in such a way that the drawing up of the sutures will cause an exact approximation of the two edges. Interrupted fine silk sutures threaded on small corneal needles are placed perpendicular to the wound so as to hold the edges together and make it watertight, they penetrate only the anterior layers of stroma. The sutures are then drawn up to demonstrate this and before being tied, their ends are passed through the conjunctival cowl. The sutures should be tied snugly but not so tightly as to invert or evert the edges. When they are tied we therefore have accurate approximation of an appreciable thickness of cornea and an appreciable thickness of sclera from the anterior surface of which all epithelium has been removed for at least 2 millimeters. The raw surface of the conjunctiva therefore has a chance to send down into these tissues new-formed blood vessels. Such an eye should be immediately treated with atropine and bichloride ointment and both eyes bandaged. It should not be re-examined for *at least* 4 days. Our recurrences are due to meddling and inquisitiveness which should not be tolerated.

If we do our surgery well, we do not have to be meddling. If we do not do our surgery well, we should quit doing surgery. Prolapses sometimes occur in the best of hands but too many of them indicate poor surgery.

One of the most embarrassing complications which we encounter is an inability to extract the lens before loss of vitreous has taken place. This may be due to an improper corneal section. Recently one of the residents who had had some experience, inserted the cataract knife back of the iris. The anterior chamber in this case was particularly shallow and a corneal section should not have been attempted in the usual way. The knife was withdrawn and the section was completed by the attending surgeon with the aid of scissors. Fortunately the Verhoeff sutures had been previously placed and were ready to be tied before the attempted removal of the lens. When the iridectomy was done vitreous presented. The speculum was removed and the eye was closed for 5 minutes. The upper lid was raised with the suture which had previously been placed in it and a DeMarr retractor was inserted. The vitreous had replaced itself, the blood was washed out of the anterior chamber and on attempting to grasp the capsule with the forceps, again vitreous presented. To go after the lens in the usual way would have invited certain disaster. Consequently a thin probe with a very smooth knob at its end was used to break a few zonular fibers at a time. In order to do this the corneal lip had to be raised very gently. The fact that vitreous presented in the wound meant that some of the zonular fibers had already ruptured. Therefore the first to be ruptured intentionally were the lower ones, then those on each side, a few at a time, until nearly all of them were ruptured, after which the lens was easily removed with the loop. The Verhoeff sutures were pulled up and before being tied, the prolapsed vitreous was very carefully excised. (One must be cautious in this maneuver as the sutures can be cut so easily.) The sutures were then tied, and with a spatula, the iris was freed from the wound.

The removal of a lens freely floating in the vitreous presents many difficulties. Particularly is this so when it does not disappear into the vitreous until after the section has been made. This can best be handled by the use of a focussed fluorescent light, or by locating the lens with the ophthalmoscope, using a fluorescent light. Great care must be taken not to injure the retina as a hole is very often produced and detachment of the retina invariably results. It is considered better surgery to leave it alone unless it can be floated

into the anterior chamber and incarcerated there by contracting the pupil behind it.

Intraocular hemorrhage on the fourth or fifth postoperative day is usually not of great import but occasionally small vessel will repeatedly bleed even after a simple iridectomy. Thorough study of the vitamin K and vitamin C content of the blood should be made. The patient's blood should be typed we have found that small transfusions of blood repeated 2 or 3 times are usually followed by very satisfactory results. The opposite treatment—preoperative bleeding—is also occasionally successful, especially if the blood pressure is elevated. Undoubtedly preoperative bleeding of the patient used to be done too frequently. I remember Dr. Casey Woods preoperative orders were frequently "Be ready to take 100 cubic centimeters of blood just before the operation."

I recall the case of a friend of mine who had a glaucoma in its early stages. He very much wished to be relieved of the necessity of using drops and as the drops did not perfectly control the tension at all times, it was felt wise to operate. A simple iridectomy was done without complications. On the second night he hit the eye with his hand while asleep and this was followed by some pain. The next morning a small amount of blood was found in the anterior chamber. The bleeding continued until the chamber was nearly filled with blood and on the fourth day a small transfusion was given him before the chamber was opened to irrigate. The transfusion was repeated and he had no further complications.

This matter of postoperative bleeding that occurs spontaneously is often of grave concern and calls for the co-operation of an internist who is studying hematology. Small transfusions of 100 cubic centimeters or thereabouts repeated daily are often of great benefit. I have not found calcium therapy as beneficial as some have claimed it to be. Should the blood remain in the anterior chamber for any length of time there results a blood staining of the cornea. I make it a practice to evacuate it about the seventh day unless by that time it seems to be disappearing.

Postoperative glaucoma is a condition that we would see less often if we would study our cases thoroughly from the standpoint of unearthing a very early glaucoma. If we find an early glaucoma I believe that it is a point of wisdom to do a deep root iridectomy preliminary to a cataract extraction. The iridectomy should be complete if it is found that the pupil will not dilate well during the preliminary study. I believe that the tonometer is not used one tenth as much as it

should be in our preliminary examinations. In this paper we cannot take up what constitutes a thorough examination of the eyes but suffice it to say that we cannot make such an examination in 1 or 2 days. When we do find that there is a postoperative glaucoma, naturally there are counteracting measures which should be taken. One of the necessary procedures is to examine the iris first with the slit lamp and a very fine beam and second, with a gonioscopic contact glass. Gonioscopy is coming into its own slowly but surely. Just as one learns microscopy first with a low power instrument, so one should learn gonioscopy first with a simple loupe and a good spot light. The higher the magnification and the more knife-like the beam of light naturally the greater the detail.

As a rule a postoperative glaucoma shows up within a month or 6 weeks after the operation. Sometimes it is brought on by continued instillation of atropine. Occasionally it can be adequately controlled by the use of a miotic. Often, however, operative measures are necessary. These measures will depend upon what one sees with the gonioscope. If the iris angle is well open and there are no peripheral synechiae goniotomy may be tried. This is a very simple operation and can be repeated many times. Often a single operation is effective. It need not necessarily be done under a contact glass but the eye must be thoroughly studied with a contact glass before it is attempted.

If a pillar of the iris is caught in the corneal wound and particularly if the anterior chamber is rather shallow, cyclodialysis seems to me to be the logical operation. This also can be repeated a number of times. We occasionally use air injections in the anterior chamber after this operation. The air should not be under great pressure but this procedure pushes the iris and vitreous away from the cornea. Occasionally a trephine is in order or an iridectomy with or without sclerectomy.

In colored people we are more apt to have complications therefore our technique must be extraordinarily accurate and delicate. In colored people we find that it is better to do no unnecessary operating.

Occasionally we have so much postoperative reaction that the pupillary area is occluded or we have had loss of vitreous and the iris is drawn well up into the wound where it is incarcerated. We like the technique of making a meridional incision in the lower iris in all cases but moderate amount of vitreous has been lost. This can be best done with the de Wecker or other very fine scissors and we do it just before the incision

is closed. It should be carried well down toward the root of the iris. When this has not been done and the pupil is obstructed by exudate or by the iris being drawn well up toward the wound, after the eye is quiet a small subconjunctival incision into the anterior chamber can be made from below and the iris root caught in a small iris forceps and drawn out so that an iridectomy can be done. The less done the less is the subsequent reaction. There should be sufficient adrenalin used before the operation so that there will be little or no bleeding into the anterior chamber.

Delirium is one of the bugbears we must all deal with. Recently a graduate of Rush Medical College, class of 1894, our history No. D-4107, a man of astonishing vitality, asked us to remove one of his cataracts. When he became delirious we removed the patch from the eye not operated upon, got him out of bed, and had his wife stay in the room with him, but all to no avail. Then I found he had been getting a barbiturate. The resident had just come on service and did not know that barbiturates occasionally cause a psychosis, particularly in elderly people. When paraldehyde by rectum was substituted he slept like a child and awoke refreshed and in his right mind.

We believe it important also to push fluids in elderly people, chipped ice, ginger ale, and often soda in small doses reduce the tendency to nausea and the tendency to dehydration. Infection is more easily prevented than combatted. We always take a culture 48 hours before any intra-ocular surgery. Small colonies of streptococci are occasionally overlooked on a 24 hour culture plate.

We lost an eye some years ago because of this and since then insist on a 48 hour culture. One or two colonies of nonhemolytic staphylococcus do not cause us concern if the eyelids look normal and if we use 1 per cent silver nitrate just before the surgical procedures are begun. It precipitates the protein in the conjunctival sac if left in the eye for 30 seconds, it can then be washed out. It tends to cloud the cornea temporarily.

We always test the patency of the lacrimal passages during our preliminary survey. Appropriate measures are taken when necessary. Should the patient have a fever or should the eye be uncomfortable during the first 48 postoperative hours we do not hesitate to remove the bandage. We first examine the dressing and secretion at the lid borders. If this examination suggests infection or if the upper lid is not normally wrinkled we carefully inspect the eye. Smears and cultures are made. Atropine and a mild antiseptic such as 1 per cent aqueous mercurochrome and bichloride ointment are used, the eyes are rebandaged and milk injections are given. With the advances in chemotherapy our methods will undergo revision, I am sure. We have given one patient sulfathiazol, another had massive doses of x-ray, the former recovered, the latter did not.

I realize that many situations can arise that are not covered by these scattered remarks. The main idea that I would wish to leave with you is that surgery should be preceded by most careful study of the patient and when surgery is attempted one should bear in mind that the eye is a most delicate structure and reacts badly to carelessness.

INFLAMMATION OF THE SALIVARY GLANDS

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AT the risk of being accused of reverting to old-fashioned nomenclature the term *inflammation*, rather than *infection*, is used in the title of this paper for the reason that some of the inflammatory conditions are caused by drugs and are not primarily caused by micro-organisms. The chief purpose of the paper is to discuss the various types of infection of the salivary glands. Until I began to realize that infection of the salivary glands ties up with and is really a part of, infection of the cervical fascia my conception of infection of these glands was indeed vague.

The process may be primary and limited to the salivary glands, or the glands may become involved secondarily in the course of a systemic disease. In the latter instance the involvement constitutes a complication, and if it occurs during an attack of typhoid fever it is none the less a case of typhoid fever and the record is filed under that heading; likewise it is none the less a case of parotitis. This makes literary investigation difficult and the witticism "always a bridesmaid never a bride" applies.

It should be remembered that there is a close anatomical relationship of the salivary gland and lymph nodes. In the case of the parotid gland some lymph nodes are situated on the capsule and some are enmeshed in the gland itself. In the case of the submaxillary gland the lymph nodes lie on the capsule. This relationship suggests that it is possible that there may be inflammatory swelling at the location of the salivary gland which may at first be wholly a lymphadenitis. I have observed inflammatory swelling over the site of these glands, parotid and submaxillary from infection in the lymph nodes without marked involvement of the salivary gland proper. Infection may involve the gland secondarily.

Some inflammations of the salivary glands, particularly the parotid, are metastatic. Osler designated these complicating and metastatic inflammations, symptomatic parotitis or parotid bubo. They are usually acute.

There are several specific types of salivary gland inflammation, chiefly mumps, mumps-parotid fever and Mikulicz's disease or syndrome.

MUMPS—EPIDEMIC PAROTITIS

A full discussion of this disease is not considered necessary but a few remarks are in order. In the first place mumps is a virus disease and is definitely epidemic. All the salivary glands may be involved or only those of one side either simultaneously or in succession. Only one gland may be involved. It is usually acute but occasionally becomes chronic due to hypertrophy. There is no suppuration. In the diagnosis it is important to ascertain the existence of any cases of mumps which the patient may have contacted within 3 weeks. An inquiry at the health department will obtain information as to the existence of known cases of mumps. It should be remembered that mumps often develops in patients after hospitalization for other reasons. In our records there are a number of instances of the development of mumps during the convalescence from injuries and operation. Obviously the contact occurred before the patients were admitted to the hospital. When the patient is in the hospital for a longer period of time the contact may be made by visitors.

It is difficult to find the records as it would necessitate perusal of thousands of histories. I was able to find the following. One case developed the day after tonsil and adenoid operation, and I am quite certain there were more. One case developed after fracture of the femur, one case after knee injury, and one 11 days after an acute upper respiratory infection. Two other cases, sisters, who were admitted to be treated for an upper respiratory infection with swollen cervical glands, developed typical signs of mumps on the day after admission.

A complicating orchitis is fairly frequent. Sometimes the lacrimal glands are involved. Rarely symptoms referable to the pancreas appear. During the convalescence of one of my deep neck infection cases, a young man at home after healing was complete, swelling of the region of the parotid gland on the same side occurred with elevation of temperature. At first it was thought that a recurrence of the deep neck infection was in progress, but in 48 hours an orchitis appeared, followed in a day or two by epigastric pain and tenderness, nausea and vomiting which were ascribed to pancreatitis. The proved contact was by a sick room visitor while in the hospital. This and the

following case history are recited to demonstrate that the complications of mumps may be formidable and may bring about severe life-long handicaps. Every otologist recognizes the importance of mumps as a cause of deafness, usually bilateral. From involvement of the testicles there may come sterility, from involvement of the ear labyrinths there may come deafness, from involvement of the nervous system—brain, or meninges—there may come death. If death occurs it is most frequently from cerebral complications.

Nervous system involvements should be accorded all the care and respect that are due any involvement of the central nervous system. The following is an example. During the past year one patient with a cerebral complication caused by mumps was treated at the New Rochelle Hospital. An adult male about 45 years of age was admitted to the hospital 10 days after the onset of an attack of mumps and 1 day after he had been allowed out of bed. On the day of admission he was suddenly taken with severe headache and vomiting which continued during the day with increasing severity. The morning temperature was normal, climbing rapidly during the day to 103 degrees F when admitted to the hospital. At this time there was also rigidity of the neck and inflammatory areola at Stenson's duct orifices. The spinal fluid showed 721 cells, 94 per cent lymphocytes, 6 per cent polynuclears, no organisms on smear or culture. By the third day the temperature had gradually come down to normal with subsidence of symptoms, and the patient was discharged at the end of 2 weeks. This patient was much depressed mentally and was considerably more ill than his chart indicated. The diagnosis was mumps virus meningitis. A prolonged rest of 3 months was prescribed.

UVEOPAROTID FEVER

Textbooks describe a condition called uveoparotid fever in which, as its name implies, there is a painless enlargement of both parotid glands with inflammation of the uveal tract of each eye. The etiology is unknown. The mortality is about 5 per cent. The swelling is firm and nodular, and usually subsides after some weeks or months. Also there is a low grade fever. Sometimes there is present one or more of the following: polydipsia, polyuria, polyneuritis, facial paralysis, burning sensation in the tongue, swelling of the lacrimal glands, and general adenopathy with splenomegaly. Visual defects are apt to be prominent and permanent. It occurs in the second and third decades of life. Tuberculosis has been accused of being the cause but this has not been proved. Treatment is purely symptomatic. The sulfo-

namide drugs might be tried. I have never seen a case of uveoparotid fever, and have based my description on what I have read in the books. My conclusion is that it is not common.

MIKULICZ'S DISEASE OR SYNDROME

Any reference to Mikulicz's disease without an expression of admiration for the masterly scientific description by Mikulicz in his original paper would be a regrettable omission. A delightful experience is in store for the physician who will take the trouble to read that paper in the original as translated in *Medical Classics*, vol. 2, October, 1937. To add to the wonder of the description, microscopic characteristics and blood count examinations were included when it was written, about 53 years ago, between 1888 and 1892.

The syndrome consists of symmetrical enlargement of the lacrimal and salivary glands and sometimes also of the accessory glands in the hard palate and tongue. Enlargement of the lacrimal glands is usually the first to appear but occasionally the enlargement of the salivary glands appears first, and sometimes only the lacrimal glands are involved. The swelling is firm, smooth, painless, not tender, and not adherent to the surrounding structures. Cecil states that sometimes there is splenomegaly and local or general lymphadenosis. Microscopic characteristics resemble lymphoma. The same source also states that in one of two cases observed there was general lymphadenosis with biopsy showing lymphosarcoma, the other patient recovering after antituberculous medication. It has occurred in diabetes. Hypothyroidism has also been observed with recovery after thyroid medication. The facial appearance is rather characteristic, almost grotesque, with the swollen eyelids, the prominent jaws and the head thrown backward for vision. Naturally the patient is not pleased with his appearance, but he complains mostly of the interference with vision caused by the ptosed and puffed out eyelids. In no instance has a definite cause been ascertained. Surgical removal in selected cases has been successful, and so also has roentgen-ray therapy.

The following is a much abbreviated summary of Mikulicz's original paper: (1) The lacrimal glands are usually involved first, followed later by involvement of the submandibulars and parotids, (2) the patient runs an afebrile course, (3) the lymphatics are not involved, (4) the spleen is not enlarged, (5) there is no leucocytosis nor other change in the blood count, (6) the disease is not a new growth, (7) the parenchymal cells (secretory) are not involved, (8) the disease is charac-

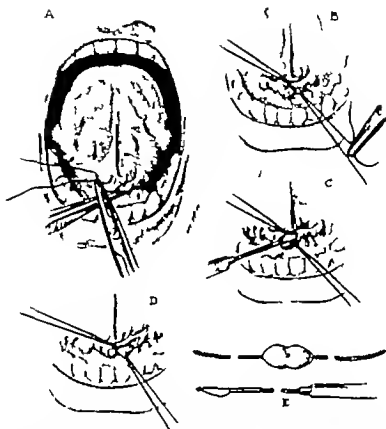


Fig. A, Manner of introducing the traction sutures. B, Traction sutures in position. Not slit shape of orifice. C, Canalliculus kind in position for slitting of duct. D, Appearance after duct has been slit open, exposing calculus. E, Instrument.

terized by a round cell (lymphocytic) infiltration in the interstitial connective tissue structure, with increase in the amount of connective tissue (9) it is essentially a chronic low grade, and not an acute process, (10) it is not systemic—Mikulicz did not consider it hematogenous in origin (11) he believed the causative factor to be "an infectious or parasitic process in the broadest sense of the word.

The editors of *Medical Classics* wrote the following summary:

"We know only that the disease seems to be a low grade infection of the lacrimal and salivary glands, extending over a long period with possible spontaneous termination and never causing death.

Little has been added to the subject since Mikulicz's contribution and the problem admits of further enlightenment. Apparently all the cases which Mikulicz observed were chronic or at

least nonacute, and the patients are otherwise apparently healthy.

Several years ago I observed a patient, a married woman aged 58 years, with a low grade nonsuppurative involvement of the lacrimal and salivary glands, but with rather acute abnormalities of their systems. I regarded the lacrimal and salivary manifestations as Mikulicz's syndrome occurring in the course of an acute illness ushered in by a severe acute suppurative and ulcerative tonsillitis.

The illness extended over a period of 4 weeks during which time there were periods of sweat dripping, bittermittent epigastric pain attributed to the biliary mechanism, and pain in the lower right chest region. There was throughout an extreme dryness of the mouth, or xerostomia, which symptom was not mentioned by Mikulicz as having been present in any of his cases. There was oral sepsis and caries of the teeth. Even during the early acute stage of the tonsillitis the temperature did not go over 101.4 de-

grees, the pulse running between 90 and 110. Both tonsils were riddled with multiple crypt abscesses, all probably connecting with each other and containing purulent exudate. There was also a vesicular rash, later becoming pustular, on the hands, chest, neck, scalp, and feet caused by *Monilia albicans* infection which yielded readily to treatment consisting of local application of gentian violet, by the dermatologist. No fungus forms were observed in the smear or the culture taken from the tonsils. Tonsil culture showed *Staphylococcus aureus* and *Micrococcus catarrhalis*. On admission to the hospital the blood indicated sepsis, with count as follows: leucocytes, 21,650, polymorphonuclears, 81 per cent of which young forms numbered 28 per cent, lymphocytes, 16.5 per cent, eosinophiles, 1.5 per cent, large mononuclears, 10 per cent, 1 metamyelocyte, toxic granules in an occasional polymorphonuclear cell, no anemia. The sepsis was attributed to the severe throat infection. It gradually subsided. Roentgenographic examination of the hilary tract after intravenous injection of dye showed failure to outline or visualize a gall bladder shadow and seemed to indicate a pathological process the identity of which was never determined. I suspect it might have been pancreatic.

On several occasions patient complained of pain in one knee joint. Blood sugar was 138 milligrams. Wassermann reaction was negative, blood culture, negative, urine sugar-free. The patient received a variety of therapy including potassium iodide, small stimulating doses of insulin, salicylates, bismuth, mixed vitamins, caroid and bile, no part of which can be said to be wholly responsible for her recovery. At first the tonsils were so swollen that they touched each other in the midline, giving rise to a type of noisy breathing with some dyspnea and at times some cyanosis. This was completely relieved by insertion of a pharyngeal airway. When the tonsillar inflammation and swelling had subsided the swelling of the lacrimal and salivary glands began to subside. She was discharged from the hospital at the end of about 4 weeks with some lacrimal and salivary swelling still present. The xerostomia was still present, but had diminished considerably. This was the driest mouth I have ever seen. It distressed the patient very much.

One month after discharge from the hospital the tonsils were removed, and since then there has been no return of the syndrome. The family doctor states that the tonsillectomy cured her. The laboratory was not requested to section and examine these tonsils, an oversight which I regret very keenly. At the time of the tonsil operation there was still present a mild xerostomia.

In the literature the ophthalmologist is the most frequently found author on the subject of Mikulicz's syndrome. This will probably continue to be the case, as the swelling of the lacrimal glands constitutes the most annoying manifestation, and ophthalmological examination is sought early. Occasionally the lacrimal glands are involved in mumps, but a diagnosis of Mikulicz's syndrome is usually justified when the lacrimal and salivary glands are simultaneously involved with nonpainful and nontender swelling. If occurring during an epidemic of mumps it should be treated as mumps. Until further enlightenment on the cause of the disease is forthcoming one cannot be more definite. Because of its microscopic resemblance to lymphoma and lymphosarcoma it has been characterized as a new-growth



Fig 2 Roentgenogram of typical small calculus in Wharton's duct on intraoral film

The evidence is otherwise against it. A point of differentiation from mumps is that with mumps there is leucocytosis with lymphocytosis. Another point is that in the absence of other conditions Mikulicz's syndrome is afebrile. Simultaneous acute inflammatory involvements elsewhere, as for example tonsillitis, would be expected to alter the blood count. For the present it may be stated that simultaneous swelling of the lacrimal and salivary glands without acute inflammation, fever, or pain, and with no related general pathology may be regarded as Mikulicz's syndrome.

INFLAMMATION OF THE SALIVARY GLANDS CAUSED BY DRUGS

Inflammation of the salivary glands caused by drugs may be acute or chronic. The parotid is most frequently involved. Involvement of the salivary glands is manifested by swelling, discomfort, and alteration of function. References to this condition in the books are found under the captions, ptyalism, salivation, sialosis, sialorrhea—synonyms for increased quantity of secretion, and xerostomia, aptyalism, oligosialia—synonyms for decreased quantity of secretion. In these cases the intensity of symptoms in the mouth from the stomatitis overshadows the symptoms in the glands. Mercurialism is the best example. As an entity it rarely needs consideration. The treatment is symptomatic and abstinence from the drug. Among the drugs that cause an increased output of saliva are mercury, gold, copper, iodine, jaborandi, muscarine, tobacco, bromides, arsenic, potassium chlorate, pilocarpine, bismuth, and lead. Among those that decrease the secretion are opiates and belladonna. Personally I have had no experience with drug poisoning. Years ago I



Fig. 3. Roentgenogram showing two small calculi in the parotid gland. Cyst shown in Figure 4, as not visible in this exposure.



Fig. 4. Roentgenogram showing large cyst in right parotid gland. About cubic centimeters of radiopaque solution as injected into Stenson's duct. Later 5 cubic centimeters of cystic fluid as aspirated, from the buccal side. Photograph slightly retouched. The cyst as excised from the mouth side.

frequently saw cases of accidental and intentional mercurial salivation: the one from continuing the use of calomel for too long periods and the other in obtaining the full effect of mercury in the treatment of syphilis. Calomel was then a household remedy and many cases of salivation and stomatitis resulted from its indiscriminate use by the layman.

ACUTE INFECTION OF THE SALIVARY GLANDS

The specific types of infection, notably mumps, are not here alluded to. There are three important types of acute infection of the salivary glands: (1) acute inflammation; (2) deep neck infections; (3) acute exacerbation of the chronic inflammation wherein calculus formation occurs; (4) acute infection occurring during the course of a systemic disease or after injury to or surgical operation on abdominal or pelvic viscera. This includes severe acute pathology in the abdomen or pelvis.

There is a rare type of acute primary suppurative inflammation, usually involving the parotid gland. It occurs in infants and young children and even in the newborn. I have never observed a case. Bock and Pacella and others have reported it in the newborn.

ACUTE INFECTION ACCOMPANYING NECK AND DENTAL INFECTIONS

In my experience acute infection in the presence of neck and dental infections is the most

common type of acute infection of the salivary glands. Its place in the picture is decidedly subordinate to the deeper cervical infection. The parotid and the submaxillary glands lie in their own compartments of the cervical fascia and are separated from each other by a union of the enveloping fascia between the glands. The external layer of the parotid fascia is very tightly fastened to the overlying superficial fascia and it is difficult to dissect the two apart. It is attached above to the zygoma for which reason swelling which involves only the parotid gland or its fascia is limited above to the zygoma. The internal surface is in relation with the sheath of the vessels, particularly the external carotid and some of its branches. The parotid gland also is in relation with small veins which enter into the formation of the common facial and external jugular veins, and less intimately with the internal jugular vein. There are a number of lymph nodes both on its capsule and embedded in its structure. Because of this contiguous vascularity and the rich distribution of lymphatics early sepsis is to be expected when it is severely involved. When infection of the parotid and submaxillary glands accompanies deep cervical fascia infection this may not be appreciated because of the already existing severe

sepsis The retromandibular process or extension of the gland forms part of the external wall of the pharyngomaxillary fossa and at its end is devoid of fascia The pharyngomaxillary fossa is divided into two unequal parts or compartments by the structures attached to the styloid process That part situated in front of these is the anterior compartment, and that behind is the posterior compartment The great vessels and their sheath are situated in the posterior compartment Infection in the pharyngomaxillary fossa quickly involves the parotid gland and when this occurs the infection is both within and without the capsule Infection in the anterior compartment of the pharyngomaxillary fossa gives an unmistakable triad of signs, viz, swelling of that lateral pharyngeal wall with protrusion inward of the tonsil fossa and tonsil, trismus, and swelling of the parotid gland If, during the course of a deep parapharyngeal infection, swelling of the parotid gland region occurs with these other signs one may be sure of infection in the pharyngomaxillary space The inflammatory swelling of the parotid gland increases the trismus and intensifies the pain on chewing because of its relationship with the neck and ramus of the jaw Otalgia is not an uncommon symptom, and for the same reason In primary inflammation, like mumps, limited strictly to the parotid gland I have never observed swelling of the lateral pharyngeal wall Swelling of contacting or neighboring lymph nodes is present and if those in the upper adjacent cervical regions are involved the parotid swelling is continuous with the cervical swelling lower down Tenderness is present over the whole area of swelling It frequently happens that abscess in and about the parotid gland ruptures into the external auditory canal I have seen this twice in deep neck infections and once when the parotid gland abscess occurred during severe inflammatory disease of the colon Simpson has reported the occurrence in pharyngomaxillary infection Sometimes a suppurative otitis media is the cause of suppurative parotitis

The treatment consists of drainage of the pharyngomaxillary abscess This is followed by subsidence of the parotid and cervical swelling, though occasionally a cervical gland abscess will form and require drainage I have not observed a facial nerve paralysis in these acute infections, though it is appreciated that such an event is possible I have seen and drained primary abscess of the parotid gland which I strongly suspected to have been entirely lymph node in origin Such infections are strictly localized The submaxillary salivary glands are more commonly involved with

lymph node abscesses than are the parotid glands In relation with the capsule of the submaxillary gland there are several lymph nodes which receive drainage from the tongue, floor of the mouth, teeth, and alveolar process of the mandible When these nodes are inflamed and swollen the appearance is the same as when the salivary gland is inflamed and swollen, in fact some inflammation of the salivary gland itself is unavoidable In practically all cases of the Ludwig's angina type the submaxillary salivary glands are involved, and sometimes during the convalescence after incision and drainage the glands are literally lying in a pool of pus Infection in the submaxillary region from whatever cause practically always involves the submaxillary salivary glands, one or both This gland is much more loosely held in its recess than the parotid gland, and as its posterior end is bent around the posterior border of the mylohyoid muscle, part of the gland is located in the mouth floor above the muscle It is to be seen that the gland may thus be a direct avenue of infection from mouth to neck From this it is also seen that it is a direct avenue of approach in the search for pus Excision of the gland is practiced as a drainage measure especially, as will be mentioned later, when there are calculi in the gland Occasionally one sees an acute infection of the sublingual salivary gland, but it is not so common It occurs with or without calculus formation The cause is not always ascertainable It may be secondary to dental infection I recently treated a patient with abscess of the sublingual gland, and no calculus nor dental pathology could be demonstrated by roentgenograms or otherwise Cyst formation, or ranula, occurs in the sublingual glands or ducts, and is probably caused by low grade chronic inflammation In Ludwig's angina with the pronounced inflammation in the floor of the mouth these glands are always involved, but this involvement is completely overshadowed Acute and chronic inflammation of the salivary glands may be caused by disease of the dental region I have seen chronic inflammation of the parotid gland, with swelling persisting for several years, accompanying dental disease for which a third mandibular molar had been extracted There occurred osteomyelitis of the alveolar process and on several occasions acute exacerbation of the chronic inflammation in the gland Figures 3 and 4 show a small calculus in the posterior part of the gland and a large cyst in the anterior part on the buccal aspect The latter shows the large cyst and the duct outlined by injected radiopaque material

I have been somewhat impressed by observance of the frequency with which dental extraction has



Fig. 3. Roentgenogram showing two small calculi in the parotid gland. Cyst above. In Figure 4, as not visible in this exposure.



Fig. 4. Roentgenogram showing large cyst in right parotid gland. About cubic centimeters of radioopaque solution is injected into Stensen's duct. Later, 5 cubic centimeters of cystic fluid is aspirated, from the buccal side. Photograph slightly retouched. The cyst is viewed from the mouth side.

frequently saw cases of accidental and intentional mercurial salivation—the one from continuing the use of calomel for too long periods and the other in attaining the full effect of mercury in the treatment of syphilis. Calomel was then a household remedy and many cases of salivation and stomatitis resulted from its indiscriminate use by the layman.

ACUTE INFECTION OF THE SALIVARY GLANDS

The specific types of infection, notably mumps, are not here alluded to. There are three important types of acute infection of the salivary glands: (1) acute inflammation in deep neck infections; (2) acute exacerbation of the chronic inflammation wherein calculus formation occurs; (3) acute infection occurring during the course of a systemic disease or after injury to or surgical operation on abdominal or pelvic viscera. This includes severe acute pathology in the abdomen or pelvis.

There is a rare type of acute primary suppurative inflammation, usually involving the parotid gland. It occurs in infants and young children and even in the newborn. I have never observed a case. Bock and Pacella and others have reported it in the newborn.

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ACUTE INFECTION ACCOMPANYING NECK AND DENTAL INFECTIONS

In my experience, acute infection in the presence of neck and dental infections is the most

tion Crile and Manning suggest that these changes, described by Bessey and Wolbach, may account to some extent for the infection in the gland

A single parotid gland is usually involved. The reasons given for the fact that the submaxillary glands are not involved are that the normal and constant motility of the tongue and floor of the mouth tends to keep the duct clear of accumulations, and also because the secretion from the submaxillaries contains mucin, a substance which has bactericidal action. The occurrence of a complicating symptomatic parotitis is always of serious significance and immediately calls for a guarded prognosis. It occurs not infrequently in the wards of a general hospital. Cecil states that the mortality is from 30 to 50 per cent. Crile and Manning had a mortality of 43 per cent in 23 cases requiring surgical drainage. In 37 patients not operated upon the mortality was 11 per cent. In 3 cases death was attributed directly to the parotitis, in 2 cases the parotitis was contributory, in the 10 remaining cases it had very little to do with the death.

The onset is sudden with increased elevation of temperature and toxemia. There is local swelling, tenderness, and pain, sometimes painful swallowing and otalgia. Crile and Manning state that "pain in the temporomandibular joint on opening the mouth is commonly the initial symptom, occurring as early as 6 or 8 hours before swelling of the gland." If not aborted at this stage there occurs redness of the skin and fluctuation from abscess formation. In 1 of my cases this redness took on a rustiness of color almost like iron rust. I have wondered whether this is to be explained on the basis of its closeness to the overlying skin just below and in front of the lobe of the ear. In another place I have referred to the difficulty of dissecting the fascia of the gland away from the overlying superficial fascia, the 2 being quite adherent. In some cases suppurative localization takes place very slowly. In others abscess formation is rapid. When abscess has formed, large incisions are not necessary provided they go through the capsule. Incision should be withheld until one is certain that there is suppuration. Spontaneous rupture through the overlying skin and occasionally into the canal of the ear occurs if incision is delayed too long. Crile and Manning state that if roentgen therapy is applied as soon as any symptoms are recognizable the prognosis is much better in that many will not go on to suppuration. They consider the x-ray treatment very important in the earliest stage, day or night. Later its efficacy is much diminished or nullified.

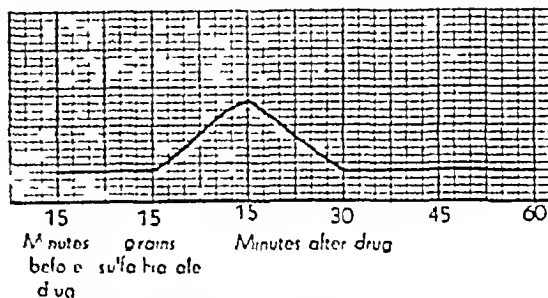


Fig. 5. Chart showing sulfathiazol concentration in the saliva with a blood concentration of 5 to 8 milligrams per cent. Note that the greatest amount appears 15 minutes after the dose was given.

Radium has also been advocated. Preoperative and postoperative oral hygiene is of the greatest importance. Cleansing of the mouth and teeth by muscular action and stimulation of the free flow of saliva, by the use of chewing gum is also of considerable value. Administration of vitamins, especially vitamin A, is also recommended because of its influence on the metabolism of epithelium. Otherwise the treatment of the parotid gland condition consists of the same measures, surgical or nonsurgical, used for any localized suppuration, but tremendously influenced by factors imposed by the primary condition. It is very advisable to begin the administration of a sulfonamide preparation 48 hours before the performance of the abdominal or pelvic operation, especially one on the colon, and to continue the administration at least that long after the operation. Since the advent of the sulfonamide derivatives, many of these dire clinical conditions should be much ameliorated, if not actually controlled, by chemotherapy.

I was able to find records of 5 cases of symptomatic parotitis in our hospital files. Our filing records do not include complications, which makes it necessary to rely somewhat upon recollection. The antecedent conditions were as follows: (1) gastric ulcer, died, (2) cesarean section with subsequent infection, died, (3) acute hemorrhagic nephritis, recovered, (4) colitis with ileostomy—parotid abscess ruptured spontaneously and healed, patient still living but very ill, (5) salpingo-oophorectomy, bilateral, also subtotal hysterectomy and appendectomy, recovered. Two of the five died.

In summing up one may reasonably state that the development of symptomatic parotitis is often contributory to the death of the patient, and always renders the prognosis of the source disease graver.

been the forerunner or instigator of infection in the salivary apparatus. Two cases, one in the parotid and one in the submaxillary gland, come to mind. They differ in no essential way from those not so provoked and are subject to the same indications so far as treatment is concerned. It is also possible that a latent dental infection, when interfered with or lighted up by dental extraction, may be the cause of the acute exacerbation. The relationship should be borne in mind. In the differential diagnostic relationship, diagnostic roentgenograms of both the ducts and glands and films of the jaw to exclude beginning osteomyelitis should be made.

ACUTE SECONDARY PAROTITIS

Oster called acute secondary parotitis symptomatic parotitis or parotid bubo. It is never primary and is always a complicating parotitis. It occurs during the severe febrile diseases such as typhoid, typhus, pneumonia, and septicemia. Now that typhoid fever is a comparatively rare disease in this part of the world, it occurs most frequently after severe debilitating abdominal or pelvic disease or injury. Oster stated that it sometimes occurs after injury disease, or temporary derangement of the genital organs, and that by temporary derangement is meant slight injuries or natural processes—a slight blow on the testis, introduction of a pessary menstruation, or pregnancy. In such cases the exact mode of involvement is obscure. In fact, knowledge of the exact pathway of involvement from the primary pelvic or abdominal disease to the gland is not yet established. Two pathways come under consideration—the blood stream and the duct system of the gland. That the blood stream is not always the pathway is indicated by the fact that the kind of infecting organisms recovered from the abscess in the gland is not always the same as the kind of organisms found in the provocative source as for example, pneumonia. Payne has made the following observation: "There is nothing in the available evidence to suggest that pneumococcal parotitis is specially prone to arise in patients with proved pneumococcal infections. When acute parotitis develops during the course of pneumococcal infection of the lung it is almost invariably caused by the *Staphylococcus aureus* and not by the pneumococcus. If the infection originates in the mouth, and it is quite likely that it does in most cases, the explanation becomes simple, but even in that event something must happen to the gland which greatly lowers its resistance and renders it more susceptible to any infection which may be present in the mouth. It is well known that in

severe debilitating illness of any kind the mouth becomes septic even when it was not septic before the illness.

BACTERIOLOGY

Members of the pyogenic group of organisms are the most frequent invaders. The staphylococcus group is found most commonly especially the *Staphylococcus aureus*. The streptococcus group is the next in order of frequency also the pneumococcus. This is to be expected as this pyogenic group is most commonly present in the mouth. The typhoid bacillus would be more commonly found if typhoid fever were now more prevalent. By way of digression I should like, while on the subject of bacteriology to refer to the types of organisms which are found in primary infections. In addition to the pyogenic group there are sometimes found fungi of which the ray fungus of actinomycosis is of particular importance in agricultural districts. In my experience here in the East actinomycosis in the mouth is very rare but it is possible that I have overlooked some cases. The tubercle bacillus and the spirillum of syphilis are occasional invaders. Because of their frequent presence in the mouth the fusil-spirochete organisms of Vincent's angina are possible invaders, though I have never actually demonstrated them in salivary infection.

That there is an element of selectivity in the occurrence of parotitis from the numerous types of abdominal and pelvic disease is suggested by the fact that it seems to be more common after surgery of the colon. Crile and Manning, in one of the best papers on this subject, reported that over half of the cases of complicating parotitis occurred after colon surgery. The incidence of parotitis in general surgery at the Cleveland Clinic was 1 in 1,500 cases. In colon surgery the incidence was 1 in 125 cases. After abdominalopereal resections of the rectum the incidence was 1 in 50 cases. They also make the statement with regard to etiology that "modern opinion favors the ductogenous theory."

Vitamin A deficiency has been shown to cause atrophy of the epithelial lining cells of many of the epithelial structures, including the salivary glands, genitourinary tract, respiratory tract, and cornea of the eye. Following the atrophy there is metaplasia from the normal stratified columnar cells into keratinized cells which desquamate and accumulate in the ducts and acini forming masses which cause obstruction. A diminished secretion and excretion of saliva results and there is dryness of the mouth. In the presence of bacteria which are present in the duct this is the start of infec-

The orifice of the duct is inflamed and prominent, and in most cases a stone in Wharton's duct can be palpated with the finger. In the case of Stenson's duct this will depend on its proximity to the duct orifice. Farther back than where the duct goes through the buccinator muscle it would probably not be palpable unless very large. Roentgenography, including exposure on an intraoral film, in my opinion is very valuable. In former years before the development of the precise roentgen technique of today it was often disappointing. Sialograph after injection of radiopaque solution, 1 to 3 cubic centimeters, has in my experience helped to differentiate between a duct and a gland calculus. It should not be done during an acute exacerbation. It is particularly helpful in the parotid duct and gland cases. I see no objection to careful probing except during acute exacerbations. It may be done in both Stenson's and Wharton's ducts, and is sometimes very helpful. If the duct is traumatized by rough manipulations an acute inflammation may be precipitated. I have recently considered the feasibility of injecting 1 to 3 cubic centimeters of a sulfonamide solution into Stenson's or Wharton's duct for these inflammatory conditions in which the calculus is in the gland or in which there is no calculus in the duct. To date I have not done so.

PATHOLOGY

Sometimes a calculus is extruded by erosion and formation of fistula, usually into the mouth but occasionally through the skin. It was submaxillary in all reported cases. If it occurs externally branchial and thyroglossal fistulas must be excluded. Calculi usually occur singly but may occur in numbers. Most of them are smooth but in one of my cases it was so rough and so firmly attached to the walls of the duct that it was necessary to detach it by sharp dissection. It had a surface similar to the rough irregular surface of an inferior turbinate bone. If the obstruction is complete, cystic dilatation of the duct behind it occurs, and congestion followed by atrophy takes place in the gland structure. In the duct itself there occur congestion, petechial hemorrhages, granulations, and fibrosis.

The following is a pathological report from one of my cases of chronic inflammation of the right submaxillary gland with calculi in the gland. I quote from pathologist's report:

"Gross examination. A submaxillary gland 6 by 4 by 2 centimeters in size. It has been cut in the longitudinal plane, exposing two small calculi deep in the substance of the gland. The cut surface is pinkish yellow in color and has coarsely lobular markings.

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"Diagnosis. (1) submaxillary gland duct adenoma, (2) acute and chronic inflammation, submaxillary gland, (3) submaxillary gland calculi."

Another of our cases carries the following histological report. No calculi were present in this one.

"Sections show greatly distorted submaxillary gland, with obliteration of gland units and productive inflammatory products between atrophic gland units. There is no evidence of tumor. Diagnosis. Chronic inflammation, submaxillary gland."

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TREATMENT

Treatment is in most instances surgical but should not be done during acute exacerbations. If there is acute inflammation hot fomentations externally with hot saline mouth wash are valuable. Administration of the sulfonamide derivatives, preferably sulfathiazol or sulfadiazine, is advisable, and otherwise any symptomatic treatment that may be indicated. Probing should not be done during acute exacerbations. When the acute attack has completely subsided, usually after several weeks, the calculus may be removed or the gland excised as indicated. For probing the duct (Wharton's) or removing a calculus I prefer to immobilize the duct at its orifice in the papilla with two silk retraction sutures as suggested by me in 1934 and here illustrated in Figure 1. Immobilizing the calculus against the inner side of the jaw with the finger, and cutting down upon it directly is the most commonly employed method of removal. When the calculus is small it is not always easily palpated, in which case cutting directly down upon it is sometimes difficult. When traction is made with properly placed silk sutures the orifice is converted into a long slit into which it is extremely

CHRONIC INFLAMMATION OF THE SALIVARY GLANDS

In the majority of instances nonspecific chronic inflammation occurs with calculus formation, and acute exacerbations take place frequently. Except during such exacerbations it causes no trouble except swelling and slight discomfort. Specific types of chronic inflammation may be caused by mumps, tuberculosis, syphilis, actinomycosis and chemicals. These also cause acute inflammations. One or more of the glands may be involved. A type of gaseous tumor formation sometimes occurs in glass blowers and wind instrument musicians. These gaseous tumors may contain purulent material.

That type of chronic inflammation occurring with calculi, either in the glands or in the ducts, is the most common. It is possible that calculus formation may be the primary condition as, for example the formation of solid concretions around a foreign body such as a seed, piece of tooth-pick, piece of fish bone, etc. In such cases chronic inflammation of the duct and gland is inevitable and sooner or later as the concretion increases in size, more or less constant or intermittent obstruction to the outflow of secretion results. The signs of obstruction are intensified during meal time when an increased amount of secretion is called forth. The signs are increased swelling of and discomfort in the gland. Sometimes there also occurs sudden filling of the mouth with a gush of released secretion. There is also swelling and discomfort in the floor of the mouth. Acute inflammation may occur suddenly with marked increase in the severity of the symptoms. Sudden obstruction in the presence of duct stone does the same.

Calculi may form during the course of a chronic inflammation and as an incident in the process. In other words it may be secondary. The same type of inflammation may not be accompanied by the formation of any calculi. It may in some instances be likened to the age-old problem of the priority of the hen or the egg. Clinically it may be regarded as the same condition whether or not calculi are present. It is probable that sometimes there is actually calculus formation present when it has not been demonstrated by diagnostic roentgenogram prior to surgery.

New and Harper have published valuable statistics on this subject. They found that in only 63 per cent of 110 cases of nonspecific chronic inflammation could they demonstrate the presence of calculi. Forty-two per cent of these were removed from the duct, 18 per cent from the gland through the floor of the mouth, and in 4 per cent the gland was excised with its calculus con-

tent. They state that clinically the condition is the same whether or not a stone is present. Statistics vary somewhat as to the relative frequency of involvement of the several glands and ducts with and without calculi. New and Harper report the following percentage of incidence of salivary calculi according to the gland or duct involved. Submaxillary gland or duct, 92.9 per cent, the parotid gland or duct, 4.3 per cent, the sublingual gland or duct, 2.8 per cent. Wakeley reported as follows submaxillary 63.2 per cent, parotid, 20.6 per cent sublingual, 16.3 per cent. Caygan reported 37 cases as follows Wharton's duct, 59.4 per cent submaxillary gland tissue, 20.8 per cent, Stenson's duct, 13.5 per cent, parotid gland tissue, 2.7 per cent, sublingual duct, 20.8 per cent Bartholin's duct, 2.7 per cent. Blair stated that the most common location of salivary calculi is in the submaxillary (Wharton's) duct, being more frequent there than in all other locations combined. That about sums it up. It occurs in middle aged people, and according to various writers, from two to five times as frequently in men as in women. Curiously the right submaxillary gland and duct are more frequently involved than the left.

In those cases of chronic inflammation without stone New and Harper report that the submaxillary gland was the most commonly affected. The incidence was as follows submaxillary gland, 80 per cent parotid gland 22.5 per cent, sublingual gland 7.5 per cent. Of the 40 there were 27 males and 13 females. In all of them tuberculosis, syphilis, and actinomycosis had been excluded as etiological factors. It should be possible to demonstrate nearly all salivary calculi by roentgenogram because they are composed mostly of calcium carbonate and calcium phosphate. It has been stated that the saliva of the submaxillary salivary glands has a higher percentage of solids and organic matter which should permit the calcium salts in these glands to be seen more distinctly than those in the calculi of the other glands. The factors which make tartar prone to form on the lingual surface of the lower incisors may also favor the formation of calculi in the submaxillary ducts and glands. A history of previous attacks, sometimes dating back years, is commonly elicited. The most prominent symptom or complaint is intermittent pain and swelling of the gland caused by acute exacerbations. Pus can be expressed from the duct by making pressure on the gland during acute exacerbations and nearly always when no acute inflammation is present if there are calculi in Wharton's duct. The same with regard to the parotid and its duct.

The orifice of the duct is inflamed and prominent, and in most cases a stone in Wharton's duct can be palpated with the finger. In the case of Stenson's duct this will depend on its proximity to the duct orifice. Farther back than where the duct goes through the buccinator muscle it would probably not be palpable unless very large. Roentgenography, including exposure on an intraoral film, in my opinion is very valuable. In former years before the development of the precise roentgen technique of today it was often disappointing. Sialograph after injection of radiopaque solution, 1 to 3 cubic centimeters, has in my experience helped to differentiate between a duct and a gland calculus. It should not be done during an acute exacerbation. It is particularly helpful in the parotid duct and gland cases. I see no objection to careful probing except during acute exacerbations. It may be done in both Stenson's and Wharton's ducts, and is sometimes very helpful. If the duct is traumatized by rough manipulations an acute inflammation may be precipitated. I have recently considered the feasibility of injecting 1 to 3 cubic centimeters of a sulfonamide solution into Stenson's or Wharton's duct for these inflammatory conditions in which the calculus is in the gland or in which there is no calculus in the duct. To date I have not done so.

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easy to pass the end of almost any kind of a small instrument. They also give good immobilization.

It should be remembered that the ranine artery, lingual vein, and lingual nerve are all on the tongue side of the duct, and therefore when working in this region one should work toward the jaw side as much as possible to avoid these structures. Excision of the submaxillary gland is the indicated procedure when the gland is severely involved, with or without calculus. This is comparatively simple but one must identify vessels and nerves, most of which are in relation with its posterior and internal aspect, namely the facial vein, the facial artery and the hypoglossal nerve. Deeply also, the lingual nerve. The facial nerve should be well out of the field. If an abscess forms it should be drained, but extensive dissection for the removal of calculi should not be done until all acute inflammation has subsided.

The foregoing applies to the submaxillary gland. The problem is more complicated in the case of the parotid gland because of anatomical location and relationships. The drainage incision for parotid abscess should never be made vertically because it will cut across the branches of the facial nerve. A horizontal incision parallels the nerve branches and avoids this. Stenson's duct perforates the buccinator muscle not far from its orifice in the mouth, and beyond this point lies between the muscle and the skin of the face. Any incision of the duct within the mouth farther back than about 2 centimeters from its orifice must involve this muscle and from the mouth aspect is deeply placed. Incision into the duct should never be made externally through the skin for fear of producing a salivary fistula, and this is to be avoided at all costs. Excision of the parotid gland is a formidable procedure and is practically never done except for malignant growths. Drainage of gland abscess should be done promptly when the indications arise. Usually small incisions that penetrate the capsule, parallel with the branches of the facial nerve suffice. The skin incision may be a single larger one. Injury to Stenson's duct must also be avoided. I have seen salivary fistula develop from a pocket knife stab wound in the sulcus between the tip of the mastoid process and the angle of the jaw. It was not in the vicinity of Stenson's duct nor did it involve the facial nerve. A wound in the gland does not always cause fistula. In that case it was decided to produce glandular atrophy by means of roentgen therapy but to date this has failed. At the time of the injury it was necessary to ligate the carotid.

The last case of acute symptomatic parotitis in our wards developed on the fourth postoperative

day. Four days later the otolaryngologist saw the patient in consultation and immediately prescribed sulfadiazine in full dosage attaining a concentration of 8.2 milligrams per cent. The swelling subsided in 48 hours without recurrence and the patient convalesced from the pelvic operations uninterruptedly. This is a striking example of the effect of the new weapon we now possess in the sulfonamide derivatives. Without their help such a case might have gone on to a disastrous septic termination or at the least a stormy septic bout. From observations made over the years before these drugs were available I have been convinced that the patient is never again the same healthy individual he was previous to the infection. It may be true that he will have acquired a more or less temporary strong immunity to the particular type of infection, but at the expense of irreparable damage to such vital organs as the heart, liver and kidneys which in time will make itself manifest. Therefore the long range effect of these drugs in cutting short these severe infections is incalculable.

After reviewing the history I had the desire to know whether or not any of the drug is excreted in the saliva, and if present the approximate quantity. With that in mind specimens of saliva were collected at intervals after the administration of the drug by mouth. The drug was given in capsules to minimize or avoid any retention of it in the mouth. We were considerably handicapped by the shortness of time at our disposal, and the following meager results are submitted in the hope that others, better equipped than we will make more comprehensive and conclusive investigations.

Our resident house officer, Dr. P. E. Noonan, made a survey of the house and from each of the patients who was receiving a sulfonamide derivative regardless of the kind of illness, collected saliva specimens of as large a quantity as the patient could produce at the following intervals of time. The first specimen was taken 15 minutes after administration, the second, 30 minutes after the third, 45 minutes after and the fourth, 1 hour after. The doses were spaced 4 hours apart. As there were too few who were being started on the drug; those who had been taking it for varying periods of time were included. As you know the quantitative estimations are done by colorimetry and in the saliva these color reactions can be seen but are too small to be measured. In other words the concentration is far less than even a low blood concentration and it is not possible to designate it in figures. It is therefore approximate in the extreme. However it was unmistakably seen that

BECK INFLAMMATION OF THE SALIVARY GLANDS

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the deepest coloration in the saliva almost invariably appeared in the first, the 15 minute specimen, but once in the 30 minute one, probably because of a slower rate of absorption of the drug in that patient. In those cases which had been receiving the drug the saliva concentration was again at the level existing prior to the administration of the dose at the end of one hour. In those receiving first dose it had completely disappeared in one hour. Nine tests were made with no variations in results.

Two conclusions may be definitely arrived at. First, there is at no time a high concentration in the saliva, in fact it is very low. Second, the highest concentration appears in from 15 to 30 minutes after administration of the dose, and quickly diminishes. From all this it may therefore be concluded that any influence of the drug on infection in the salivary glands comes from the concentration in its circulating blood, and that any influence from that in the salivary secretion is practically negligible. How much, if any, may accumulate in the gland secretion when there is obstruction to its outflow is not known. On the other hand it may be definitely stated that there

is a very small amount of the drug in the saliva while it is being taken by the patient. In other words the secretory cells of the glands do pass some of it through.

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REFINEMENTS OF GENERAL SURGICAL TECHNIQUE AS APPLIED TO OPHTHALMIC OPERATIONS

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In a consideration of the evolution of modern ophthalmic surgery in relation to general surgical technique, it is often merely inferential to associate certain ocular surgical techniques with the practices of the general surgeon. However, most ophthalmic surgeons obtained their early training in general surgery and undoubtedly received their first inspiration from the masters of general surgical technique.

The practice of eye surgery is based upon the same 3 fundamentals governing general surgery (1) the control of hemorrhage, (2) the proper anesthesia and (3) the prevention of infection. Improved methods of controlling hemorrhage and better anesthesia have made the rapid skillful eye surgeon whose surgical judgment may not have been too good, less important than the thoughtful, careful but possibly less brilliant technician. Better methods of preventing infection have greatly lessened deformity and blindness from this source. That modern ophthalmic surgery owes a great debt to the pioneers who dared to break away from the routine, conservative and often antiquated practices to undertake new methods and new techniques in surgery is evident. We know that Harvey who discovered the circulation of the blood, received the ridicule of his colleagues; he and his followers were called "circulators" which meant quacks and charlatans. The men associated with the development of ether anesthesia had tragic fates with the exception of Long.

Pasteur who destroyed the theory of spontaneous generation and laid the foundation for the prevention of operative and postoperative infection, worked for years without recognition. Unless Lister had been prepared to receive the message of Pasteur and carry on his work of preventing wound infection in spite of the active opposition of his colleagues, he would never have introduced the Listerian principle of antiseptic surgery, upon which modern ophthalmic surgery is founded.

To determine exactly where credit is due for present day ophthalmic practice is difficult, for many surgical procedures are of ancient origin.

For example ligature for the control of bleeding in wounds was used by the Greek and Roman surgeons. Therefore one is inclined to agree with Ambroise Paré, who said "you will have to render an account not to the ancients but to God for your humanity and skill."

ANESTHESIA

General anesthesia has been and still is of great importance in the development of ophthalmic surgery but for most operations local anesthesia is preferred. Before a general anesthetic is administered it is advisable to quiet the patient by the use of chloral and bromide by rectum or by the administration of morphine and hyoscyne.

Flagg's intratracheal inhalation anesthesia is a valuable improvement in administering ether. It has facilitated the performance of delicate eye operations, as recession and cataract, as it eliminates disturbing head movements and congestion of the eyes, and lessens the danger of lung infection.

Rectal anesthesia with avertin (19, 77) is especially useful in ophthalmic surgery in preventing fear of operation in young children.

Intravenous anesthesia with evipan (sodium evipan) has been used in paracentesis, enucleation, excimeration, cataract, trephining, iridectomy for acute glaucoma, exenteration of orbital growths and squint (56). However cases in which vomiting (5) sneezing, sobbing, and postoperative restlessness occurred have been reported. When intravenous injections can be made, this anesthetic is satisfactory for short operations (72).

Local anesthesia with cocaine applied to eye surgery through the brilliant research of Koller was undoubtedly even more important for ophthalmology than general anesthesia. Cocaine is still used in ophthalmic operations when vasoconstriction and dilatation of the pupil are desired. Because procaine is less irritating than cocaine and produces less drying of the epithelium, a one per cent solution of this drug (78) is gaining popularity as a local anesthetic for eye surgery.

The development of procaine (novocain) which is much less toxic than cocaine (16) led to the more constant use of deep injections about the eye for anesthesia and akinesia. A solution of procaine and adrenalin is employed in Grädle's application

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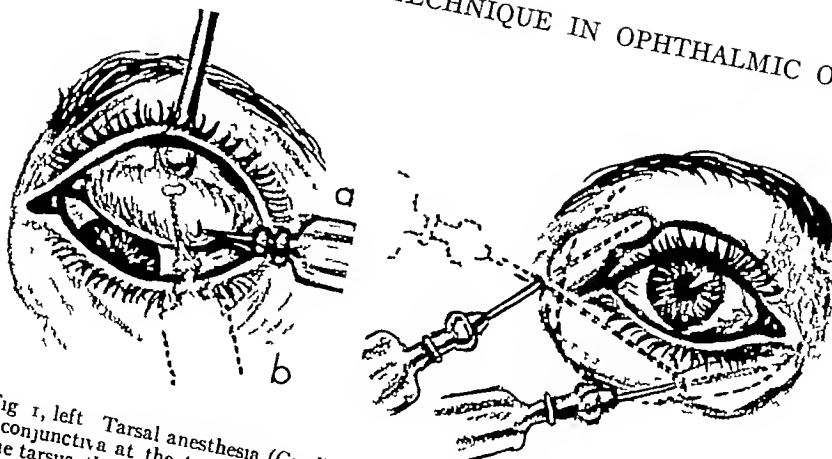


Fig 1, left Tarsal anesthesia (Gradle) *a*, The point of the needle is introduced through the conjunctiva at the temporal edge of the tarsus and passed parallel to the upper edge of the tarsus, thus ballooning out the retrotarsal fold *b*, The needle is pushed slightly toward the skin side, thus thoroughly anesthetizing the entire eyelid including the skin and conjunctiva

Fig 2 Modification of the Van Lint method of producing akinesia

of the method of nerve block anesthesia (31) to surgery of the eyelids (Fig 1) In this procedure, the point of a 25 gauge hypodermic needle is introduced through the conjunctiva at the upper temporal border of the tarsus One or 2 minims of a solution of procaine and adrenalin is injected at this site and the needle is passed forward parallel to the edge of the tarsus, thus ballooning out the retrotarsal fold

In spite of the numerous advances in anesthesia, the ophthalmic surgeon still awaits the development of a pill or capsule which will cause rapid, prolonged anesthesia without complications

AKINESIA

Modification of Van Lint's method of producing akinesia Because Van Lint's splendid method of akinesia sometimes produces too great and prolonged relaxation of the eyelids, the following technique has been developed A 26 gauge needle, 25 millimeters in length, is inserted subcutaneously 8 millimeters temporal to the external canthus The needle is pushed forward as the plunger forces the procaine (2 per cent, 2 drams) and adrenalin (3 minims, 1 1000 solution) under the skin of the upper eyelid as shown in Figure 2 The needle is then partially withdrawn and inserted in the lower eyelid, ballooning the tissues over the outer third of the lower eyelid A second puncture is made at the center of the eyelid, 3 millimeters above the orbital margin, and the needle directed toward the inner canthus, thus the solution balloons the skin In the *O'Brien method of akinesia* (49) the point of injection is just anterior to the tragus of the

ear, below the posterior portion of the zygomatic process and directly over the condyloid process of the mandible From 1 to 2 cubic centimeters of a 2 per cent solution is injected at a point directly over the exit of the branch supplying the orbicularis, while the remainder is injected superficially under the skin and spreads fanlike, in a forward direction, above and below the eyeball (Fig 3) When a patient has an extremely broad face, complete akinesia may not be produced by the O'Brien method, even with a second or third injection In this event, the modification of Van Lint's method of producing akinesia is indicated However, the more remote the site of the injection from the field

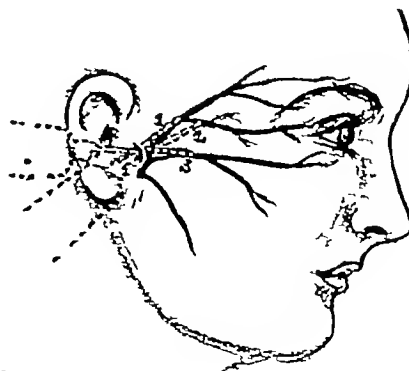


Fig 3 O'Brien method of akinesia Injection of the upper, 1, middle, 2, and lower, 3, branches of the seventh nerve

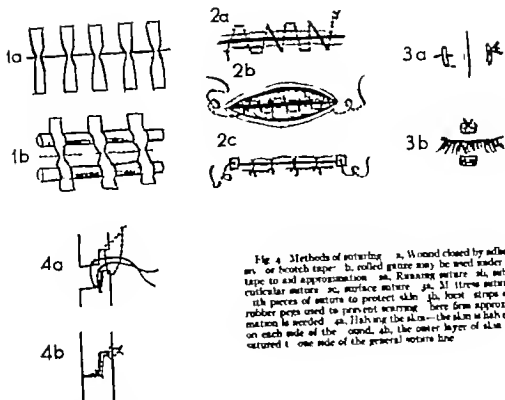


Fig. 4. Methods of suturing. a, Wound closed by adhesive or Scotch tape. b, rolled gauze may be used under tape to aid approximation. 2a, Running suture. 2b, subcuticular suture. 2c, surface suture. 3a, 3b, Stress suture. 3b, pieces of suture to protect skin. 4b, loose strips or rubber pegs used to prevent scarring. 4b, loose strips or rubber pegs used to prevent scarring. 4b, loose strips or rubber pegs used to prevent scarring. 4b, loose strips or rubber pegs used to prevent scarring.

of operation, the less the danger of complication therefore the O'Brien skinless is preferable to the injection of the eyelids, especially for plastic operations

INCISIONS

Knowledge of the healing of skin incisions dates from the time of Hippocrates, who operated for calculi in the kidney by incision. Dioscorus Cynastus (circa 350 B. C.) bandaged the head for wounds caused by darts. Theodoric (150) of the order of the Preaching Friars taught that wounds should heal by first intention and that suppuration was unnecessary. As it is so well established today it seems impossible that Paracelsus had to fight for this principle as late as the sixteenth century.

Wounds were closed by adhesive strips and by rollers and compressors until animal gut sutures were employed by Rhazes (A. D. 850). Physick (1768) experimented with bookstring, French kid and animal gut as ligatures. In 1848 W. T. Wright wrote on the use of sutures in surgery and their advantages over adhesive strips and other modes of coaptation of the edges of wounds. Adhesive tape and Scotch tape still have their uses. Because

there is little danger of death from the separation of eye wounds, the use of adhesives as advised by general surgeons (23) is valuable in primary and secondary wound closure when fear or shock is to be avoided. It is usually advisable to cut a notch in each side so that the strip will be narrow here it crosses the wound. If the tape is flamed, it usually holds better.

Postoperative scars. Ophthalmic surgeons have learned much concerning the prevention of scarring from the teachings of general and plastic surgeons. For example (1) The incision must be made with a sharp knife and part of a safety razor blade is advised by the plastic surgeons to insure a sharp edge. However since cataract knives may be sharpened so well, many ophthalmic surgeons use these knives for other than cataract incision. (2) The incision should not cut across the skin and must not be beveled because epidermis

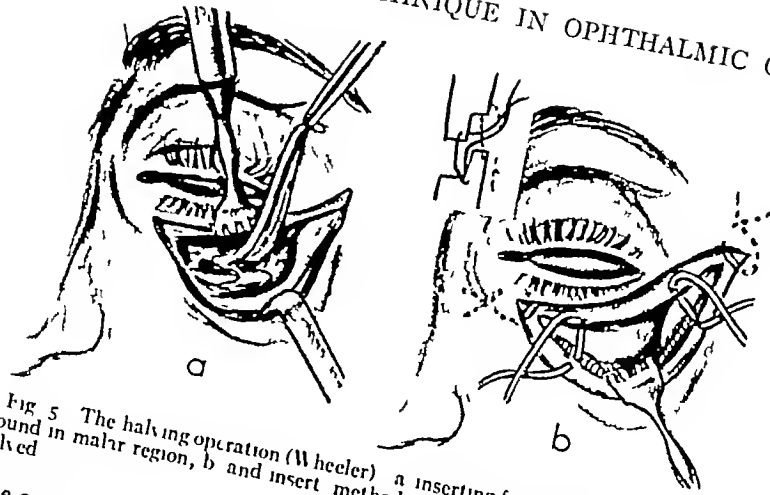


Fig 5 The halving operation (Wheeler) a inserting fascia lata in depressed wound in malar region, b and insert method of suturing skin which has been halved

after the layers of the corium have been accurately approximated, excellent results are obtained. However, there is usually some uncertainty about suturing the different levels of the skin accurately, and halving the skin, as suggested by the general surgeons, permits accurate approximation of the epidermal layers. On one side of the incision the outer half of the skin is excised and on the other side the inner half of the skin is removed. These incisions of the skin need be only a few millimeters in width, the wound edge on which the deeper tissue has been removed is drawn over the surface of the wound edge, the outer surface of which has been removed (Fig 4).

Wheeler used the halving operation for lower eyelid and malar bone deformities (Fig 5). After proper coaptation has been obtained, infection is the most serious danger to healing and each stitch should be observed daily. Keloid is particularly disfiguring and the general surgeons have pointed the way here by suggesting excision and radium treatment (61).

SUTURES AND SUTURING

Largely because of the delicacy of ophthalmic surgery, needles and suture material have been constantly improved. Most ophthalmic hospitals now have a traumatic needles available in various sizes, threaded with fine catgut and No 000,000 to No 00,000,000 white and black silk. Mersutres on curved eye needles, No 000,000 black gossamer silkworm, have been useful in plastic surgery of the eye. I have found nylon sutures of value in transplanting Tenon's capsule (7) and in resection (4) and retroplacement operations (9) for strabismus, nylon sutures have also been found of value for closing skin incisions.

Much of what ophthalmologists have learned concerning the use of new suture material has been derived from their general surgical application, for example, the dangers of catgut. In the time of Lister, catgut had been tried often and as often abandoned. The factors governing the loss of strength of catgut when embedded in tissue were pointed out by Howes. He found that (1) in the presence of fluids such as physiologic sodium chloride solution or of blood serum, the tensile strength is moderately diminished, (2) in an inflammatory exudate composed in large part of phagocytic cells, plain or chromicized catgut, practically irrespective of size, loses tensile strength with great rapidity, (3) when infection is foreseen or when the premature loss of tensile strength in the catgut would be disastrous, removable nonabsorbable tension sutures are indicated as an adjunct to the closure of the wound.

When enucleation was performed the fact that suppuration often followed and that difficulty arose in obtaining complete closure of Tenon's capsule led to the conclusion that the catgut was often unsterile and that its use did not permit complete closure of Tenon's capsule.

The idea of not burying catgut was first brought to my attention when I observed gynecologists (30a) closing abdominal wounds. This principle has been applied to the enucleation operation (6). One needle of the double-armed suture of No 5 parafinized black silk is then passed through Tenon's capsule into Tenon's space. A purse-string suture is placed within Tenon's capsule and includes the tendons of the recti, care is used not to overlap the edge of the capsule. The ends of the sutures are then knotted over a rubber tubing and the

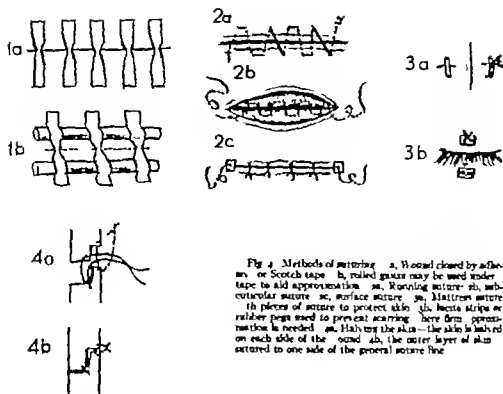


Fig. 4. Methods of suturing. a, A wound closed by adhesive or Scotch tape. b, rolled gauze may be used under tape to aid approximation. 2a, Running suture. 2b, subcuticular suture. 2c, surface suture. 3a, Mattress suture. 3b, pieces of suture to protect skin. 4a, Incision strips or rubber pegs used to prevent scarring. 4b, here firm approximation is needed. 4a, Half way the skin—the skin is half on each side of the wound. 4b, the outer layer of skin sutured to one side of the general suture line.

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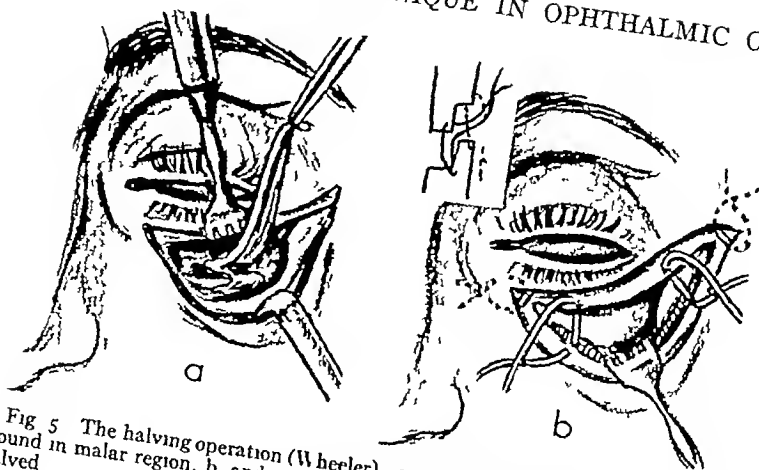


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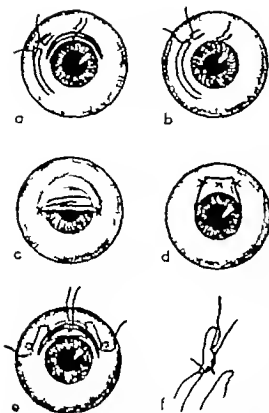


Fig 6 Methods of closing cataract wounds. a, Willson conjunctival suture (1897) b, Kalt corneoscleral suture (1894) c, Van Lint conjunctival flap d, Barraquer (1933) and Green (1931) conjunctival apron e, Berens remaining conjunctival and episcleral suture (1935) f, McLean corneoscleral suture (1940)

conjunctiva is closed by means of interrupted plain silk or catgut sutures. Only the deep sutures are removed. This technique has been used in more than 60 enucleation operations and post-operative loss of the implanted foreign substances has been less frequent than when catgut sutures were buried. The plastic implant (10) has been expelled in only 2 cases.

Although surgical wounds have been closed with sutures for years ophthalmic surgeons have been slow in suturing cataract wounds. However the use of sutures in this operation has been almost universally adopted in the United States of America since the discussion of this subject before the American College of Surgeons in 1925 by Zentmayer Posey Ellett, and the author at that time there was great difference of opinion in regard to the value of suturing. Ellett championed the K

suture the author the conjunctival episcleral suture whereas Zentmayer and Posey opposed the use of sutures. At that time none of the surgeons at the New York Eye and Ear Infirmary was employing sutures, except occasionally in complicated cases. Now in the majority of eye hospitals in the United States, sutures are used routinely for cataract extraction and several refinements have been suggested (Fig 6).

The principle of not using tension in suturing has been applied to cataract wounds for too much tension causes overlapping of the scleral and corneal wound edges.

STERILIZATION OF INSTRUMENTS AND DRUGS

By 1895, chemical sterilization had been replaced by dry heat and steam sterilization, except in the preparation of the skin and of the operating field.

Moist dry heat method. This method is satisfactory for the sterilization of eye instruments. Thoroughly cleansed dry instruments are placed in open boxes in an electric sterilizer (Moria) and the door is left partly open until a temperature of 180 degrees F (80 degrees C.) is reached, to be sure the instruments are dry. The boxes are closed and wrapped in paper and the door is shut when the danger of retained moisture with rewetting radiation is past. When 335 to 345 degrees F (155 to 160 degrees C.) is reached, this temperature is maintained for 30 min. Sets of instruments may be kept sterile for 1 week. If wrapped boxes are dated, the differentiation of sterile from non-sterile instruments is facilitated. Single instruments and syringes may be sterilized in large glass test tubes closed with cotton. The principal objection to the dry heat method is that several sets of instruments are required.

Chemical sterilization. For the chemical sterilization of instruments M. H. Post has used solution of alcohol 95 per cent with liquid cresols compound 2 per cent. Others, commercial chloroform 2 ounces liquid boric acid 1 dram. With these chemicals no rust or tarnish appears on the blades after many days.

Buffer eye solutions for surgical use and their sterilization. To lessen congestion of the eyes in operating it is well to use solutions which are nonirritating. A refinement of general surgical technique is Gifford's method of buffering eye solutions (29). The composition of the acid buffer solution No. 1

Boric acid (anhydrous)
Potassium chlorate
Distilled water

100 ml
100 ml
100 ml

100 ml
100 ml
100 ml

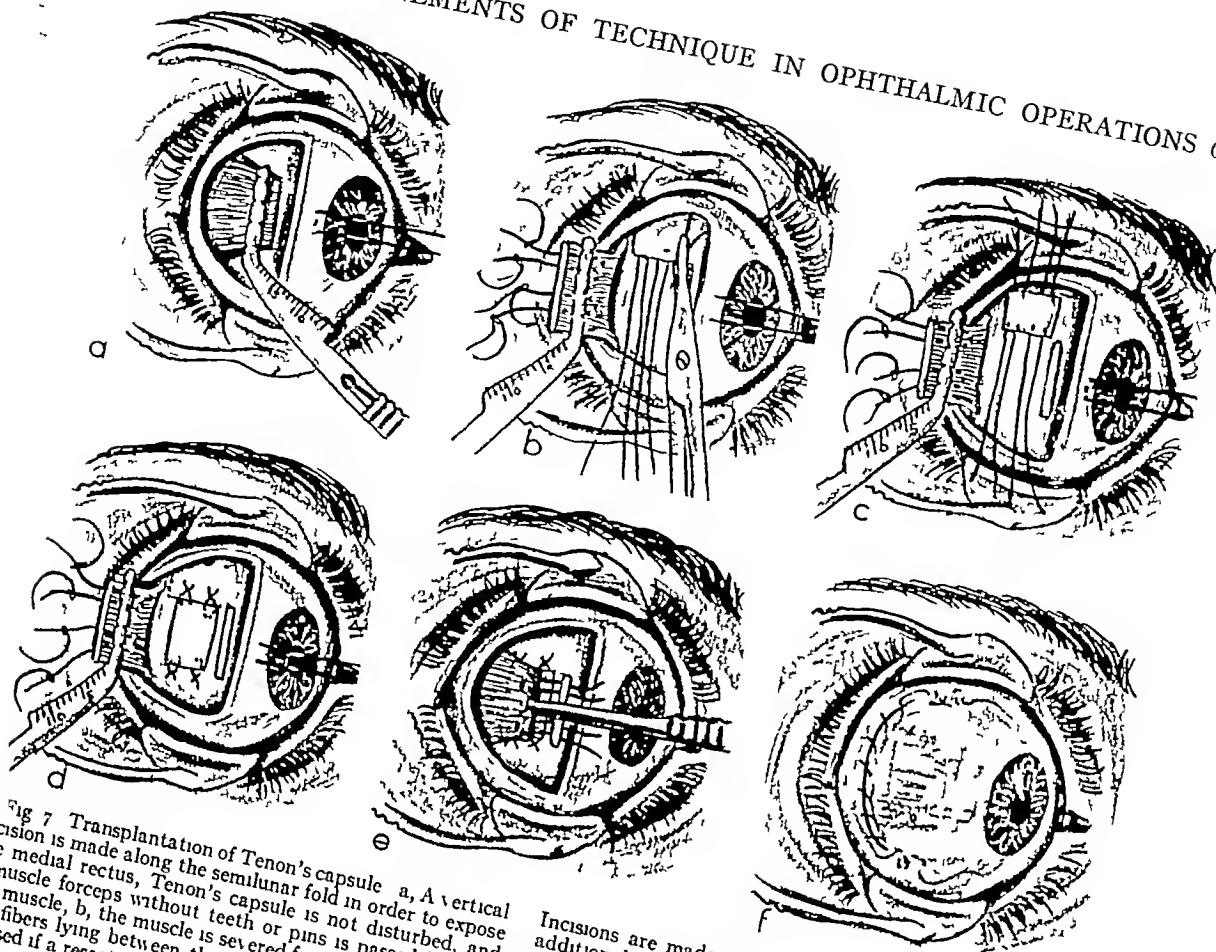


Fig 7 Transplantation of Tenon's capsule a, A vertical incision is made along the semilunar fold in order to expose the medial rectus, Tenon's capsule is not disturbed, and a muscle forceps without teeth or pins is passed beneath the muscle, b, the muscle is severed from its insertion, and the fibers lying between the forceps and the insertion are excised if a resection is desired. Two double armed sutures are passed through the muscle from the scleral surface and then through the holes in the forceps. Tenon's capsule is undermined on one side of the muscle and two double armed sutures are passed through the border of the capsule

Incisions are made on each side of the sutures c, Two additional sutures are passed through Tenon's capsule and the graft is freed, d, Tenon's capsule is reversed and sutured with episcleral sutures over the rough scleral area where the medial rectus was formerly adherent e, the medial rectus is drawn over the graft by means of traction with fixation forceps after the sutures have been passed through the muscle stump, f, the conjunctival wound is closed with a running suture. It is possible at this point to see the muscle and the graft in outline through the conjunctiva

The composition of the stock sodium carbonate solution is
Sodium carbonate (anhydrous)
Distilled water

Gifford's acid buffer solution No 2, which is suitable for cocaine and epinephrine, is made by adding 0.05 cubic centimeter of the stock sodium carbonate solution to 30 cubic centimeters of acid buffer solution No 1. His alkaline buffer solution No 1 is made by adding 1.5 cubic centimeters of the stock sodium carbonate solution to 30 cubic centimeters of acid buffer solution No 1. It is suitable for atropine, homatropine, pilocarpine and physostigmine. Alkaline buffer solution No 2

21.2 gm
1000 c c

is made by adding 4 cubic centimeters of the stock sodium carbonate solution to 30 cubic centimeters of the acid buffer solution. It is useful in cases of vernal and chronic conjunctivitis.

Preoperative preparation of the conjunctiva. To sterilize the conjunctiva the antiseptics used should be selected according to the organisms found on smear and culture but a 0.25 per cent solution of zinc sulphate is useful as a routine procedure. In certain cases 1:2500 metaphen instilled several times a day has been helpful. Silver as suggested by Bell has been used with apparent success in lessening postoperative infection in catarract operations. Excellent results are likewise claimed by certain surgeons (11), who use no anti-

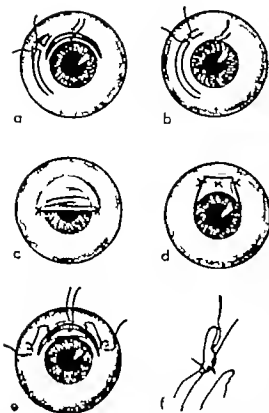


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Morris dry heat method This method is satisfactory for the sterilization of eye instruments. Thoroughly cleansed dry instruments are placed in open boxes in an electric sterilizer (Morris) and the door is left partly open until a temperature of 180 degrees F (80 degrees C) is reached, to be sure the instruments are dry. The boxes are closed and wrapped in paper and the door is shut when the danger of retained moisture with resulting oxidation is past. When 335 to 345 degrees F (155 to 160 degrees C) is reached, this temperature is maintained for 30 minutes. Sets of instruments may be kept sterile for 1 week. If wrapped boxes are dated, the differentiation of sterile from non-sterile instruments is facilitated. Single instruments and syringes may be sterilized in large glass test tubes closed with cotton. The principal objection to the dry heat method is that several sets of instruments are required.

Chemical sterilization. For the chemical sterilization of instruments M. H. Post has used a solution of alcohol 95 per cent with liquid cresols compound 2 per cent ounces, commercial chloroform ounces, liquidabolene 2 drams. With these chemicals no rust or tarnish appears on the blades after many days.

B. Fertig eye solutions for surgical use and their sterilization To lessen congestion of the eyes in operating it is well to use solutions which are nonirritating. A refinement of general surgical technique is Gifford's method of buffering eye solutions (29). The composition of the acid buffer solution No. 1 is

Boric acid (anhydrous) 4 grs
Potassium chloride (anhydrous) 7.4 grs
Distilled water q.s.

This is suitable for phenacaine and betyn.

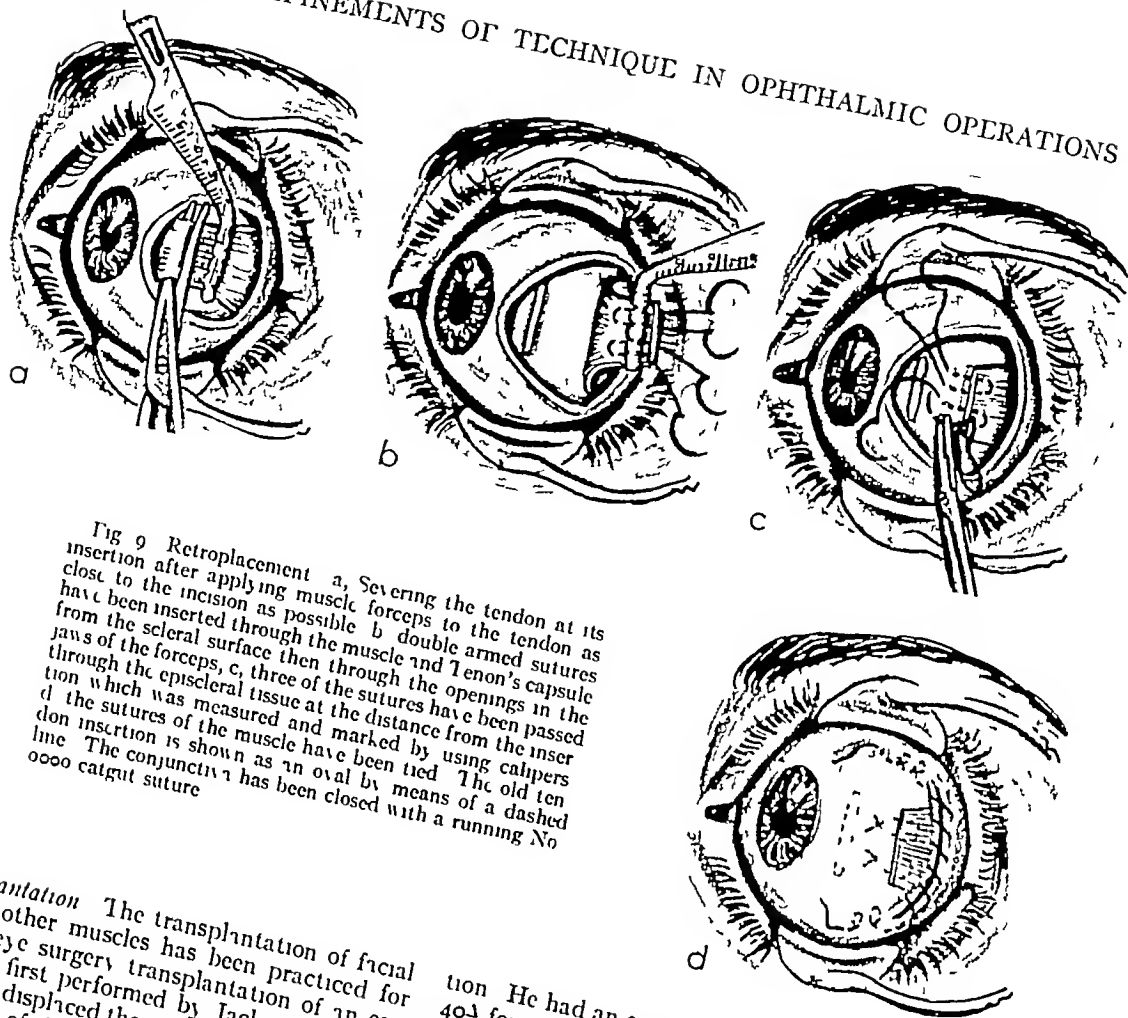


Fig 9 Retroplacement a, Severing the tendon at its insertion after applying muscle forceps to the tendon as close to the incision as possible b double armed sutures have been inserted through the muscle and Tenon's capsule from the scleral surface then through the openings in the jaws of the forceps, c, three of the sutures have been passed through the episcleral tissue at the distance from the insertion which was measured and marked by using calipers d the sutures of the muscle have been tied The old tendon insertion is shown as an oval by means of a dashed line The conjunctiva has been closed with a running No 0000 catgut suture

Transplantation The transplantation of facial muscle or other muscles has been practiced for years In eye surgery transplantation of an eye muscle was first performed by Jackson when he receded and displaced the superior rectus laterally for paralysis of the superior oblique

Gifford (30) believes that transplantation of living tendon slips from the superior and inferior rectus muscles offers the best chance of a cosmetic and functional result in paralysis of the lateral rectus muscle

A brilliant result was obtained by me in one patient (Major I L), who had a paralysis of the sixth nerve, and was referred by Dr Daniel B Kirby Transplantation of the lateral half of the superior and inferior recti with Tenon's capsule to the attachment of the lateral rectus, combined with a 6 millimeter resection of the medial rectus, was performed Binocular single vision was obtained and he was admitted to the Civilian and American air forces Before operation his vision was 20-15 in each eye without correc-

tion He had an esotropia of 45Δ for distance and 40Δ for near At the last examination he measured an esophoria of 10Δ for distance and 5Δ for near His vision was normal in each eye and no lenses were prescribed At the time of the patient's first visit, he complained of diplopia and at the last visit he could hold binocular vision a little beyond the midline in the field of action of the paralyzed lateral rectus

PLASTIC OPERATIONS

With the advent of Listerian antiseptic procedures, it became possible to repair hitherto permanent disfigurements of the body Some surgeons began to treat these cases by utilizing living bone, cartilage, and flesh It was World War I that made a specialty of plastic surgery

Cartilage transplantation Von Mangold in 1897 first advocated the use of a section of cartilage to support the interior prominence of the nose Bone and cartilage are used for the purpose of reconstructing mesodermal structures Cartilage possesses the lower metabolic rate (66) and unpre-

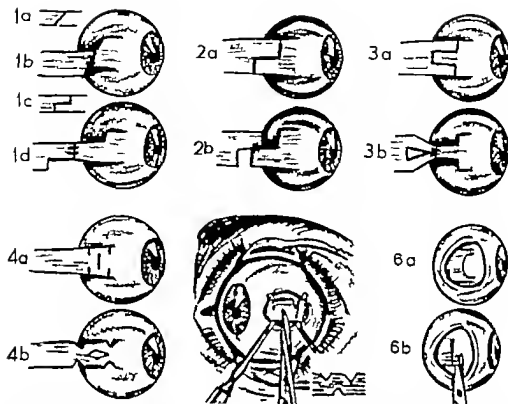


Fig. 8. Tendon lengthening by division of tendon. Stephenson method: 1a, b, division and lateral displacement of tendon; 1c, step division, suturing of upper and lower cut edges; 1d, anastomosis method; 2a, step-like division; 2b, reattachment of muscle; 3, Grissdale method; 3a, tongue flap division; 3b, sutures introduced through extreme cut edges; 4, Verheeff method; 4a, 4b, pair of vertical incisions through one fifth the breadth of the tendon at the upper and lower borders, and critical incisions made; 5, between the incisions through the middle quarters

of the tendon; 5, Todd method; 5a, tendon is stretched between two strabismus hooks, and incisions are made through one third of the tendon; 5b, the upper border and one incision made through one third of the tendon at the lower border; 6, O'Connor 0-staple tenotomy; 6a, central tenotomy is performed leaving short margin of millimeters; 6b, after 4 weeks tenotomy of the millimeter bands which are left attached at the upper and lower borders is performed.

septica on the conjunctiva before operation because they assert that asepsis of the conjunctiva is probably maintained by the lysozyme of Fleming when it is contained in the tears in normal concentration. Antiseptics possibly decrease the concentration of lysozyme by increasing lacrimation. Atropine by producing paralysis of the parasympathetic nerves, diminishes lacrimation and increases the concentration of lysozyme.

MUSCLES

The prevention of adhesions following muscle operations probably originates from the covering of intestinal wounds to prevent adhesions. In eye surgery this principle has been recently applied (7) to the prevention or treatment of adhesions be-

tween the muscles of the eyeball and the sclera (Fig. 7). The results in 9 cases have been most encouraging, although in one case the first operation made the condition worse and this has not been rectified. In another patient the first operation also made the condition worse, but a second Tenon's capsule transplant which was performed at the insistence of James W. White and Daniel B. Kirby resulted in improvement in motility and appearance.

Tendon lengthening has been used for weakening eye muscles for years; the first attempts following the principles used in general surgery (Fig. 8). However, this procedure has been almost completely discarded in recent years for recession (17, 38) and retroplacement (9) (Fig. 9).

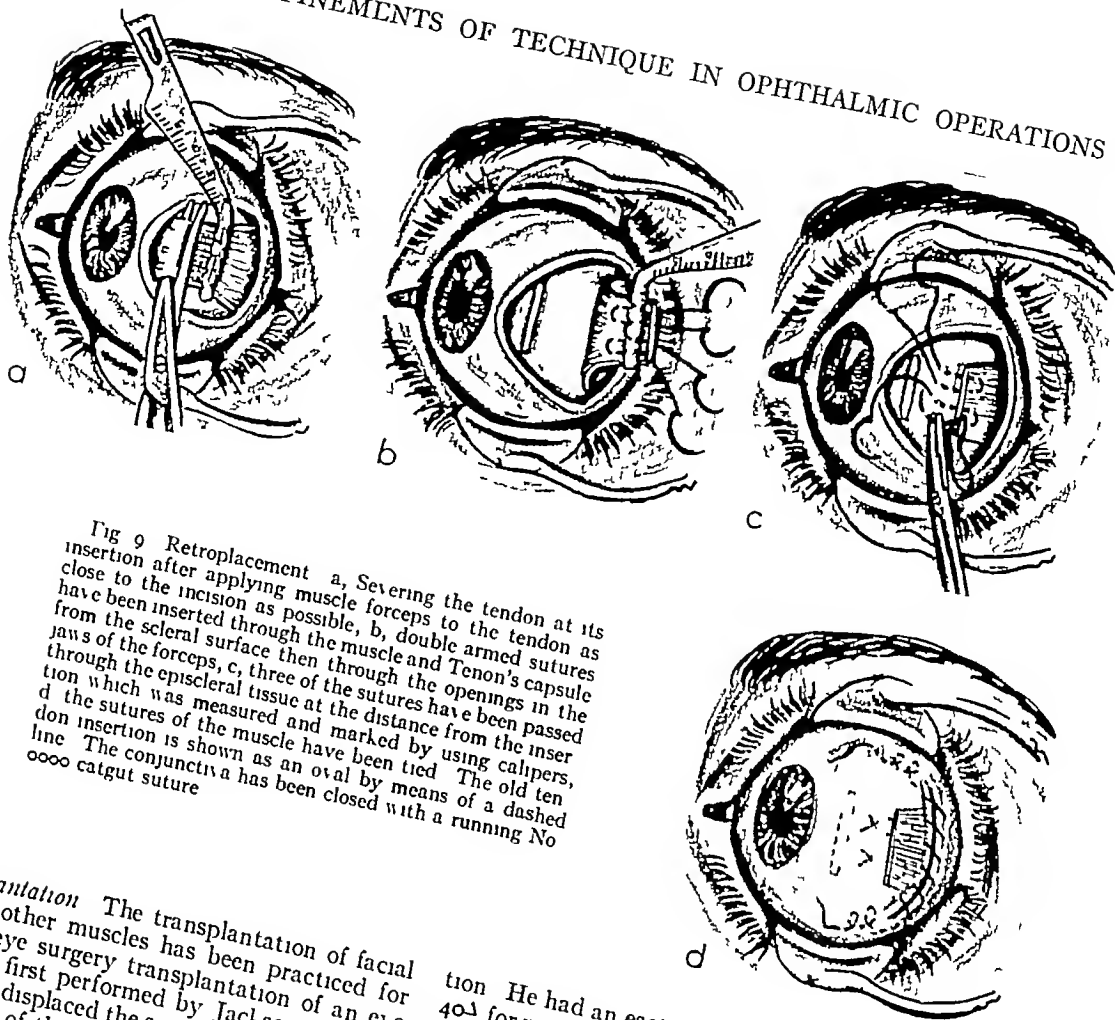


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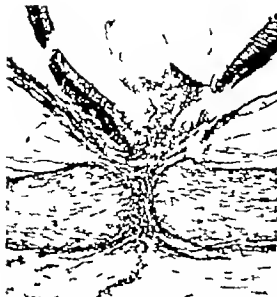


Fig. Eschar proliferation through electrolysis puncture made in the eye of rabbit. Note from localized necrosis present after 8 days.

served autogenous cartilage may return to a normal state (Loeb). Autogenous costal cartilage transplantation so far has been used by ophthalmologists mainly for filling in depressions about the orbit, and as an implant after enucleation. Cartilage ("pickled" in 90 per cent alcohol) remains as tolerated dead foreign bodies (homografts) for about 9½ months (51).

Autogenous cartilage from the ribs, survives after transplantation, as living cartilage up to periods as long as 6 years, neither increasing nor decreasing in size. Obtaining the cartilage, however, is not without risk. Therefore costal cartilage obtained during autopsy has been advocated by Struth and Slaughter in cases in which the cause of death is known and in which the deceased person's blood is serologically normal. Middle aged persons are preferred because their cartilage does not present too much fibrous tissue or too much calcification.

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Fascia. Fascia has been shown by general surgeons to be a living tissue, and has been used for the correction of paralytic mouth deformity and for filling depressions. Fascia is used in ophthalmology for filling in depressions which need not

be too resistant to pressure as those in the malar region, not involving the orbital margin. Fascia is used for correcting ptosis (41) for the correction of strabismus (28) to line scleroplasty and keratoplastic conjunctival flaps (57) for paralytic lagophthalmos (75) as subconjunctival grafts (74), and for replacing the tarsus.

Preserved fascia lata is claimed to be as useful as fresh tissue and Ellett (20) has used it for the correction of ptosis with varying results.

Grafts. Plastic surgeons have taught ophthalmologists many ways of using different types of grafts. Although Szymanowski in 1867 wrote the first thorough book on restorative surgery it was not until 1871 that Reverdin introduced the circular epidermal skin grafts.

The Thiersch graft was introduced in 1886 and proved that comparatively large pieces of skin could be transplanted. These grafts consist of very thin strips of epidermal skin taken from the extensor surface of the arm or the anterior region of the thigh. The Thiersch razor, an ordinary razor or grafting knife may be used to remove the strips but I have found that more uniform and thinner grafts may be obtained with the Padgett (52) dermatome. The technique I have found useful in restoring the socket is as follows: The socket is prepared as advised by Weeks (71) and Wheeler. The eyelids are undermined to the orbital margins. Kerr's dental compound wrapped in a Thiersch graft is inserted after the canthotomy.

Gillies has used the *Esmer epithelial inlay* (72) for contraction of the outer canthus.

Wolfe of Glasgow 1876 also utilized fairly large free skin grafts. The piece of skin was cut from selected parts of the body preferably the outer side of the arm. Its size was about one-third larger than the size and shape of the area to be covered. Weeks (72) used the Wolfe graft for restoring the lower eyelid, obtaining the graft from the inner surface of the upper arm. When possible it seems preferable to obtain the skin from the upper eyelid as the color is better.

Pedicle grafts were used by Kaspar Tagliarozzi and described in his book entitled *De Chirurgia per insulionem* (597). He restored the entire nose by means of a double pedicle flap taken from the arm. Pedicle flaps have been used for coloboma, and the correction of permanent fistula of the eyelids.

Blair and Brown prefer a skin graft of intermediate thickness for certain plastic procedures, for example the back of the hand not over the knuckles and on the subcutaneous muscles of the face and orbicularis oris and palpebrum.

Blanket grafts A method of skin grafting which is termed "blanket graft" by which a graft with a total area of 176 square inches is prepared, has been described by McPheeters and Nelson. In their technique a pattern of the area to be covered is made by tailoring a sheet of gutta percha to fit it exactly, and this sheet in turn is covered with the thinnest grafts obtainable with the Padgett dermatome. The individual grafts are then sutured.

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There can be little doubt that the use of free grafts by general surgeons inspired the attempts at total (58) and partial (35) corneal transplantation. Usually the grafts have been obtained from enucleated eye and transferred immediately but grafts from cadavers have been advocated by Ilatov. A transplant was taken from the eye of a cadaver 41 hours after its enucleation. In his case the tissue remained transparent during 41 months of observation. Eyes for this purpose are enucleated 2 hours after death and kept in a refrigerator at 5 to 6 degrees centigrade.

GLAUCOMA

There are some points of similarity between intracranial hypertension and glaucoma and the surgical treatment used by neurosurgeons and ophthalmologists. In 1865 Dr Julio Sola employed a trephine to drain a penetrating head wound. Who can doubt that the trephine operation for glaucoma really had its inspiration in the work of Sola, Elliott and Irgens were the first to use a trephine for the removal of a segment of the cornea in operations for glaucoma. There is a marked similarity between the strange iridosclerectomies and the trephine

There is a marked similarity between the La grange iridoclerectomy (39) and iridocorneoscler ectomy (4) and subtemporal decompression (18). However, according to Hirtmann (34), La grange developed his technique without knowledge of Cushing's work, although one might surmise that there was a relationship.

Although one might surmise that there is a relationship formerly in the treatment of brain abscess, trephination and drainage by means of wicks were employed Mosher's drum 1926, was a real advance. This operation may be compared with since This operation may be compared with indolitis (13) and with the drum operation of Francosa is well as the seton operation (89) and the Wiener drainage operation Wiener put a thread between the choroid and the sclera (70).

ALCOHOL INJECTIONS

In 1903, Schlosser used alcohol injections for trigeminal neuralgia. In 1915, Sicard (62) injected alcohol into the nerve trunk of the median nerve in cases of painful lesions of the nerve plexus. In 1928, Weckers called attention to the sedative

action of the intraorbital injections of alcohol. He referred to the work of N. Bruce in 1913, Brady in 1915 and others who showed the value of anesthetics in inflammations.

Ciliary ganglion Magitot injects 1 to 1.5 cubic centimeters of 20 to 50 per cent alcohol into the ciliary ganglion in cases of iritis, iridocyclitis, glaucoma secondary to iridocyclitis, interstitial keratitis (syphilitic), phlyctenular keratitis in children, and acute glaucoma even with good vision. I have used 1 cubic centimeter of 80 per cent alcohol in absolute glaucoma with high tension and pain. The pain and tension have been relieved in several cases. I inject 1 cubic centimeter of novocain, 4 per cent, with 3 minims of 1:1000 adrenalin in the region of the ciliary ganglion. The needle is left in place, after 5 minutes the alcohol is injected.

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For pain and glaucoma, Alexander rejected the resection of the ciliary ganglion and Grueter's injection of alcohol into the orbit around the ciliary ganglion on account of their risk and adverse complications, i e., paralysis of ocular muscles, perforation of sclera, possible necessity for enucleation, pain. He found that injections of alcohol into the gasserian ganglion gave great satisfaction in neuralgia of the trigeminus, as there were no ill effects.

Fifth nerve and gasserian ganglion. Schloesser, Ostwalt, Levy and Baudouin and Sicard (62) were among the first to inject the nerve-trunk in trigeminal neuralgia. Groves has recommended the injection of the branches of the trigeminal nerve with 80 per cent alcohol. This is done through a long needle thrust into the cheek so as to be above the sigmoid curve of the jaw, and an endeavor is made to enter the foramen ovale or the sphenomaxillary fossa, in order to inject the actual nerve trunks near the ganglion.

Supraorbital neuralgia. The

headaches were treated by Sweetlow with relief for 10 to 12 weeks, by alcohol injections of the great occipital or supraorbital nerve.

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Sphenopalatine ganglion. Pain produced by ker-
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photophobia, blepharospasm, and lacrimation.
Various methods of anesthetizing the sphenop-
alpine ganglion are as follows:

4. Local application - Bismuth is used for a variety of purposes. It is applied to the skin after a burn or scald to soothe the pain and to prevent infection. It is also used in the treatment of various skin conditions, such as eczema and psoriasis. Bismuth is also used in the treatment of various internal diseases, such as ulcers and gastritis.

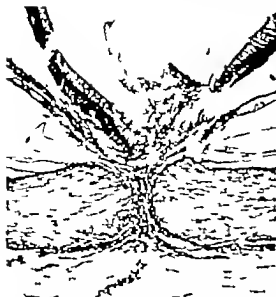


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Supraorbital neuralgia Three cases of supraorbital headaches were treated by Swetlow with 10 to 12 weeks, by alcohol injections of the occipital or supraorbital nerve.

Sphenopalatine ganglion Pain produced by iritis, iritis, glaucoma, and other ocular conditions may be controlled by anesthetizing the ganglion or by intraorbital injections. In a case of photophobia, blepharospasm, and lacrimation, Magitot's methods of anesthetizing the sphenopalatine ganglion are as follows:

A. Local application—Bonain's solution (alcohol, carbolic acid) is applied with a cotton applicator directly or after cocaine 4 to 5 per cent. The applicator, slightly bent, is introduced between the middle turbinates, following the lower edge of the turbinate until its posterior end is reached.

pellicular is rotated slightly outward and is pushed little further allowing it to rest on the fossa containing the sphenopalatine ganglion for a minute.

B. Injection of the sphenopalatine ganglion.—A 1% novocain injected directly in the sphenopalatine ganglion, through the greater palatine canal, injection should be made in the mouth at the level between the second and third molars here the canal merges into the gum. A thin angulated syringe is used with 35 millimeter rather blunt needle. Some novocain is injected under the mucous membrane of the mouth, the needle is then pushed into the greater palatine canal (35 mm. deep) and 0.5 cubic centimeter of 1 per cent solution of novocain is injected. It is inadvisable to inject alcohol because some cases of necrosis of the maxilla have been reported, probably because the palatine artery was injured.

Spastic entropion. The injection of alcohol for the correction of spastic entropion has been advocated by several ophthalmic surgeons. The skin about the external canthus is painted with 3 per cent iodine and 0.5 cubic centimeter of a 4 per cent solution of novocain, is injected into the outer fibers of the orbicularis muscle extending a distance of about 4 or 5 millimeters into the lower eyelid near the margin. The needle is left in place and 0.2 to 0.3 cubic centimeter of an 80 per cent solution of alcohol is usually injected into the muscle. (I prefer 0.5 c.c. of 80 per cent ethyl alcohol.)

INJECTIONS FOR PAIN IN HERPES ZOSTER

According to Secunda, Wolf and Price in 13 of 15 patients with acute herpes zoster relief from pain was obtained by injections of 0.5 per cent to 1.0 per cent novocain followed as necessary by nupercaine. Hollander's formula or a modification of it, thus:

Benzocaine
Benzyl alcohol
Phenol
Oil of sweet almond q. ad

While pain disappeared promptly it recurred in some patients from 1 to 30 hours later. Injections of novocain and the anesthetic in oil permanently abolished the pain in 7 of 9 patients. The areas of herpetic hyperesthesia are mapped out by pin prick, brush or pinching, cleaned with 95 per cent alcohol and subcutaneously infiltrated with the therapeutic agent until there is total anesthesia.

SCLEROSING INJECTIONS FOR ANGIOMAS

There can be little doubt that the injection of sclerosing solutions for varicose veins (27) and hemorrhoids led to the use of these solutions by ophthalmologists. Forester who made the first injections recommended sodium salicylate, quinine, and red mercuric iodide. The reaction (venitis) which leads to obliteration and secondary

atrophy of the superficial vessels is now usually produced by sodium chloride, sodium molybdate, monoethanolamine oleate, 66 per cent solution of dextrose.

Malkin has successfully injected hemangioma of the eyelid with sclerosing solutions (e. g. quinine and ethyl carbamate, quinine dihydrochloride, sodium chloride).

ELECTROSURGERY IN THE EXCISION OF TUMORS EXENTERATION AND DETACHMENT OF THE EYELID

The experiments of d'Arsonval and Oudin led to the use of electrosurgery in 1907 and diathermy was first employed in eye operations in 1911. In 1929, Moers described the use of the diathermy knife for orbital phlegmon. He believes that the advantages of this method are (1) pain is eradicated without opening blood vessels or lymphatics and (2) the diathermy incision produces sterilization along the line of incision and of the tissues a certain distance from the point of application. Monbrum has given the following indications for coagulation: exenteration of the orbit for a large invading tumor as well as destruction of tumors or other chronic proliferations of the eyelids and the bulbar conjunctiva.

In performing exenteration of the orbit, Mc Reynolds also prefers the electrocautery knife which reduces to a minimum the hazard of spreading the cancer cells.

Diathermy has been most successfully applied to operations for retinal detachment, and the majority of surgeons in the United States of America (8) prefer it. Safar used a diathermy current of about 30 milliamperes, small needles about 1.5 millimeters in length placed over the retinal tear then over the entire area of the detachment. After all the needles are placed and the current is applied, he removes them, thus allowing free escape of subretinal fluid. Some surgeons prefer the Lacarrere needle, Walker pins, or the Graefe curved needle applicator and about 40 milliamperes of current.

ELECTROLYSIS

Electrolysis, so long used by dermatologists for the removal of superfluous hair is especially useful to remove cilia. I prefer to use 0.5 milliamperes for 1 minute. Electrolysis was first used in operations for retinal detachment by Verboeck in 1911. In my experience (8) and from animal experiments (Fig. 10) electrolysis makes a more firm union between the retina, choroid and sclera than does diathermy. In applying electrolysis in the macular region I have found that the delicate platinum

needles of Walker, 15 milliamperes for 3 seconds, are useful I prefer to use the Grieshaber steel needles, 5 milliamperes for 5 seconds, in the peripheral parts of the retina

SUMMARY AND CONCLUSIONS

Although some surgical practices seem to have originated with ophthalmic surgeons, most of their procedures seem to be adaptations or refinements of general surgical technique. Special consideration is given to the following: anesthesia, incisions, sutures and suturing, sterilization of instruments and drugs, muscles, plastic operations, glaucoma, alcohol injections, injections for pain in herpes zoster, akinesia, sclerosing injections for angiomas, electrosurgery in the excision of tumors, exenteration, detachment of the retina, and electrolysis.

Although Ambroise Paré said we will have to give thanks to God for our humanity and skill, the ophthalmic surgeons should also thank the general, neurologic, and plastic surgeons for much of their success in attaining the hippocratic ideals of ability, grace, speed, and painlessness.

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RECENT TRENDS IN THE SURGERY OF HETEROTROPIA

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THE operative treatment of heterotropia has recently completed its one hundred and second year. On October 26 1830, Dieffenbach, inspired by Strohmeier's ideas and following Delpach a technique for tenotomies, performed the first squint operation by cutting the internal rectus of the right eye in a boy of seven. Since then much has been written on the subject. At first there was an almost unbelievable mania for operating on cross-eyed individuals, and tenotomies and myotomies were done by the thousands in all parts of the world with the inevitable bad results. There followed the usual reaction of skepticism. The improvements in surgical technique by von Graef and others throughout the nineteenth and at the beginning of the twentieth century did not seem able to overcome that reaction, and in 1905 Haab is quoted as having stated that "the operation for the correction of strabismus is the least satisfactory of all operative procedures on the eyes" (83). Landolt mentioned the fact that an old practitioner and professor of ophthalmology had given the surgical treatment of strabismus up completely on account of its unsatisfactory results. But Landolt himself did not agree with that attitude toward the operative treatment of heterotropia and emphasized that bad results were a consequence of not adhering to the fundamental surgical principle "Understand the nature of the disease we attack. Understand the way operations work." Much good clinical and surgical work has been done since in the field of surgical treatment of strabismus, chiefly in Anglo-Saxon countries, and Landolt's advice seems to have been followed as much as possible. Consequently the results of that treatment have improved continuously.

Strabismus, according to William Thornwall Davis, is really a complex of diseases having one common symptom, namely the deviation of the eyes from their parallelism. Better understanding of this complex of diseases is responsible for the establishment of general rules for treatment to be applied intelligently in each individual case. Surgery is a very important part of that treatment although one should always bear in mind that "to

employ the highest type of surgery is but to take a small step toward the production of a physiological result" (Nugent). This small step, however, is in many instances absolutely necessary and it seems to be an accepted rule that when strabismus does not show any improvement after a reasonable trial period of 6 months (Wilkinson) with medical and orthoptical treatment or if such improvements come to a standstill, there is no other alternative but to operate. Duane's statement that "temporizing treatment with prisms and exercises has very decided limitations should never be forgotten. Worth-Chavasse added to Duane's caution "temporizing treatment must now be recognized for what it is—fiddling while Rome burns."

There does not any longer seem to be serious controversy regarding the necessity for early treatment of strabismus nor regarding the aim of the treatment—namely to establish simultaneous binocular stereoscopic vision. It is true too that when operations have to be resorted to, they are but one phase of the treatment, preoperative and postoperative orthoptic medical treatment being equally essential in order to get good physiological results. It is an equally accepted truth that the medical treatment of heterotropia succeeds in greatly reducing the proportion of surgical cases.

As Lancaster has recently emphasized accurate knowledge of the nature of the extraocular muscles, of their form and functions is of great importance for the complete understanding of the surgical treatment of heterotropia. As he has pointed out, it is essential to know that weakening or strengthening one given muscle is not the purpose of an operation for the correction of strabismus. The real aim of such procedure is to place the eye in a more favorable position for synergic movements with the fellow eye to enable simultaneous macular perception fusion, and stereoscopic vision. One should never forget that there is a great disproportion between the power of each muscle and the energy actually needed for the movement of the eyeball; consequently the idea of strengthening or weakening simply one muscle cannot prevail.

In order to be able to choose the best surgical procedure it is of great importance to investigate the nature of each case of heterotropia and never to neglect consideration of convergence and di-

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Recently Harms, Herlyn and Renner made a survey of a series of strabismus patients in central Europe who had already been operated on, and found that very few patients indeed could be spoken of as physiologically cured. In an overwhelming majority of cases there was a more or less perfect anatomic cure. As Harms pointed out, this was due to the fact that the approach to the significance and essence of concomitant strabismus is not sound and many ophthalmologists still abide by Wiesel's ideas expressed as follows: "The surgeon performing an operation for strabismus does away with the pathological alterations found in the eye and thus serves cosmetic purposes which are so generally welcomed nowadays."

Experimental pathological investigation in order to verify histologically the result of surgical methods has been done to a small extent. It can be readily understood why such investigation cannot be easily carried further with human eyes. Consequently the source of our knowledge must of necessity remain in the clinical field. Thus it would be of great advantage to the progress of our knowledge if ophthalmologists could be induced to give the subject of strabismus more care, so that so much of their efforts would not be completely lost. Only analysis of the end results of many well observed cases will enable us to judge the advantages of a particular method and for that purpose a fixed criterion for gathering the data for such papers should exist. A comparatively large number of instructive papers dealing with the treatment of strabismus and meant for doctors who are not ophthalmologists, and even for the lay public, have been successful in increasing the number of cross-eyed children being given proper care. In the same way possibly something could be achieved to educate ophthalmologists.

In spite of the great difference in standards, by and large considerable progress in the surgical treatment of concomitant strabismus may be noted, and it is to be hoped that with an increasing number of cases coming for early treatment, as a result of the enlightenment of the general practitioner and the lay public, more will be achieved in the near future.

Regarding the surgical treatment of paralytic strabismus, in comparison there has been more progress in the last few years, as can be readily inferred from the increasing number of papers (the majority of them very good) dealing with this subject, which are found in the literature. This growing interest in the surgical treatment of paralytic strabismus is most desirable because as it has been pointed out by Gifford (28) there are still many ophthalmologists who give the matter

little or no attention, and moreover our approach to the subject will undoubtedly benefit from the gathering of new data.

Differences of opinion still prevail to a large extent regarding the choice of the operation for each type of case. This seems to be due more to a lack of proper diagnosis, quite difficult in many instances, than to actual individual disagreements. The paralysis of an external muscle can easily cause a contraction of its opponent or an overaction of its synergical associate muscle in the contralateral eye and the predominance of the latter or of the former action can give a rather confusing picture. If the real cause of the deviation is not discovered, improper treatment will follow with all of its evil consequences, including the discrediting of a good method.

The exact diagnosis is sometimes really difficult to establish. Sound knowledge of all the muscular functions, more especially in the several directions of ocular gaze as it was emphasized by Vander Hoeve and Rockers is a condition *sine qua non* of success.

Generally speaking there are already some accepted rules for the choice of the operative method, as Peter has pointed out, and these rules are the result of constant observation. But regarding what can be expected from each type of surgical treatment there is still some controversy (Gifford, Bielchowsky et al.) The same controversy prevails in relation to the possibility of transplanting the tendon of a lateral rectus to a spot a few millimeters above or below its former attachment for the purpose of correcting vertical deviations (Casten, Mikuni). There is also a difference of opinion regarding the action of transplanted tendons of abducting muscles. Experiments in *anima vili* (Olmstead, Marguti and Yanagisawa, 72) seem to prove that such transplanted muscles can thereafter have an adducting action, while others (Beard) deny that possibility. Equally controversial is the matter of priority in the surgical treatment of combined vertical and lateral deviations. White (79) is in favor of correcting the vertical deviation first whereas others prefer to correct both lateral and vertical defects simultaneously. The importance of vertical deviations has been emphasized too (Harms, 33) especially in children in whom its early correction has been advocated (Kroeckmann) in order to prevent torticollis with its injurious results in the development of the skeleton. Anatomical findings of absent muscles (Casten) and of muscular bands under the contracted rectus internus (Apple) which cannot be suspected before the operation also have been reported.

I shall now proceed to review the several advances in the surgical treatment of heterotropia reported in the literature on the subject from 1937 up to 1940. The year of 1937 has been chosen because a very complete review of the literature up to that date was published by C. Maynard Wheeler in that year.

The prevailing views on the several aspects of the surgical treatment of heterotropia according to the literature in the last few years follow.

Age at which to operate. It appears that in the United States there is an almost unanimous view regarding the question of age as a limitation for the operation of strabismus. Operative treatment should be resorted to whenever found necessary, if the medical orthoptic treatment did not bring about any improvement after a trial period of 6 months, irrespective of the patient's age.

The principal reasons given in favor of an early operation are (a) greater response to postoperative orthoptic treatment in younger patients, and (b) the disadvantage of having a physically handicapped child mentally influenced by that handicap (Dunnington).

There are still quite a number of opinions in favor of a late operation, chiefly in Europe. The explanation for those opinions are chiefly (a) the advantage of operating with local anesthetic, this being only possible after adolescence, (b) the possibility of spontaneous cure before adolescence, (c) the difficulty in securing the parents' permission to operate early. Spontaneous cure appears to be very rare indeed, the straightening of the deviated eye at adolescence proving with hardly any exception only an anatomic cure with binocular vision practically always absent.

Regarding the parents' unwillingness to grant permission for the operative treatment, it is a matter of education, and according to the suggestion of Martin and Nugent, both the medical profession and the laymen should be instructed about the advantages of early treatment, operative or otherwise. Regarding the anesthetic, general anesthesia is finding greater favor in strabismus operations at all ages.

Choice of cases for operation. All cases of divergent concomitant strabismus, not responding in a short time to medical orthoptic treatment, are surgical cases. In convergent heterotropia, opinions vary as to the maximum degree of deviation justifying conservative treatment. Some go as far as to advise surgical treatment for all cases above 8 degrees (Sternberg), others to state that under 15 orthoptic treatment alone is adequate. Here again it is rather hard to establish a fixed limit based on the degree of deviation for operative and

nonoperative cases. As long as there is marked and continuous improvement with orthoptic treatment, operative treatment should be postponed. Whenever there is a high degree of hypermetropia great caution is advisable even if full correction of the existing ametropia fails to correct the tropia immediately, a belated improvement may still be expected and consequently surgical treatment should wait (Dunnington).

OPERATIVE PROCEDURES

There are several types of operations for heterotropia. Some aim at increasing the effect of the muscles, and others at decreasing it. Among the operations of the first group are the advancement of the tendon and the shortening of the muscle, or the combination of both types, as in advancement with resection. The advantages and disadvantages of each group will be discussed later.

The different types of operations should not be used indiscriminately. If individual preferences for a particular surgical procedure are put aside when the preference seems to have no special basis, there are definite reasons for the chosen methods of treatment of the several types of strabismus.

According to Gibson there are three main causes of bad results in the surgical treatment of heterotropia, namely overcorrection, undercorrection, and choice of the wrong type of operation. Hence, it is important to choose the type of operation most adequate according to the exact findings and measurements in each individual case.

Some controversy seems to prevail regarding the importance of measuring the actual strength of each individual muscle in order to choose the operation in the different cases. Lancaster does not pay much attention to the action of each individual muscle, whereas others still attach great importance to it and even go to the extent of testing the strength of the muscle at the beginning of the operation in order to decide the type of surgery ultimately to be used (Jameson).

The relative state of convergence and divergence appears to be of major importance in the choice of the operative method (Maxwell Langdon, 42, Peter, 54, Dunnington). According to Prangen (59) increased esotropia at the near point is a sign of excess of convergence and increased esotropia for distance is a sign of excess of divergence. Conversely, decreased esotropia at the near point is a sign of lack of convergence and decreased esotropia for distance is a sign of lack of divergence. Accordingly, in cases of excess of convergence the interni should be weakened, in cases of excess of divergence, the abductors should be

weakened in cases of lack of convergence in convergent strabismus, an operation strengthening the external should be preferred. In cases of lack of convergence in divergent strabismus an advancement of the internal should be chosen. In cases of lack of divergence strengthening of the abductors is the method of choice.

More and more the idea prevails that the action of the operative treatment should be equally divided as much as possible between the two antagonist muscles of the same eye, in order not to have too much tension in the sutures which might cause ultimate changes in the results (Curly Berens, 12; Kilwan). Gibson was led to favor this idea too by the good results observed in cases of very great deviations in which this method of operating simultaneously on two muscles of the same eye had been used.

A careful examination of each individual patient is essential for the proper diagnosis of the actual cause of the "symptom." And this diagnosis is absolutely necessary for the choice of the proper operative method. Guller classified the several types of strabismus and their respective aspects in the different tests. Thus, the test for visual acuity will spot all cases of amblyopia; testing the movements of the eyeball will show the difference between a pseudoparalytic strabismus and that of heterotropia due to underaction or overaction of individual muscles; the use of atropine rotates the eye inward in the pseudoparalytic and decreases the deviation in the accommodative type. The correction of ametropias with proper glasses will decrease the deviation angle in both accommodative and anisometropic type; measuring the angle for the near-point and for distance enables the separation of the muscular from the accommodative types; the tests for fusion will show a certain degree of fusion in the accommodative type, fusion for larger images in the anisometropic, partial fusion in the amblyopic, and none at all in the fusion type.

When double hyperphoria (Verhoeff) is found simultaneously with lateral deviations it is very important to have that corrected either before or at the same time as the lateral strabismus.

Simple tenotomy. Simple tenotomy nowadays had better be mentioned in the historical part of the surgical treatment of heteropia, for there is no possible difference of opinion regarding the unpredictable effects of this crude and unscientific method. Both experimental work and clinical investigation have proved without any possible doubt how unreliable the method is. A few surgeons still use simple tenotomies, but the only acceptable reason for its use is the fact that it is

very simple, lending itself to easy performance on young children. However, the possibility of hampered convergence resulting from tenotomy on the internal recti of young children is one of the principal reasons why the operation should not be used.

In the surgery of divergent strabismus, simple tenotomy of the external rectus is still advocated, but logically a recession would replace the simple tenotomy very advantageously.

Controlled tenotomies. In order to avert the dangers of simple tenotomy, several methods have been devised by which a stitch is passed through the muscle or the tendon before it is severed, this stitch being tied afterward to the tendon stump on the sclera, to the conjunctiva, or both.

Von Blascovics described technique for a controlled tenotomy and his method has found great favor in central Europe (Hanna, 33; Miklos). Von Blascovics' controlled tenotomy is quite an improvement upon the more primitive procedure of simple tenotomy, but neither this method nor any other presented so far can compare with Janssen's recession, the tendon of the severed muscle not being properly attached to the sclera and consequently the final attachment being somewhat uncertain and unpredictable. The favor met by controlled tenotomies can be ascribed to the possibility of subsequent improvement of the results of an operation when overcorrection or undercorrection are found to be present. This is achieved by leaving the sutures tied in a way that allows for the tightening or the loosening of the suture in the first days after the operation. More will be said about this presently.

Weakening of muscular action through other methods than tenotomies. Lengthening of muscles is seldom used any more, but occasionally the method is mentioned in the literature. Samurawitz recently advocated lengthening the muscle by pulling hard at it with a strabismus hook. He associates this with advancement of the antagonist. Central tenotomies are still practiced here and there but their use does not seem justified since, as it has been proved by the experiments of Watrous and Olmstead, this type of operation is effective only because the postoperative attachments to the sclera of the part of the tendon operated upon bring about reduction in the arc of contact. Peter has deliberately reduced the arc of contact by suturing the tendon to the sclera some millimeters back of the point of normal attachment. Alabaster with gold sutures pulls the muscle in the opposite direction of its action during the advancement of the antagonist, and Worth-Chavasse places a band of electrocoagulation

not exceeding 1 millimeter at the bottom of a deep groove of the same width with the purpose of converting the contractile portion of the muscle in front of the band into inert tendon, thus reducing the action of the muscle. Walker, who studied histologically the muscles after this sort of diathermocoagulation, found that both the nerves and the muscular fibers are destroyed. By and large these different methods have not met with great favor and too little is known about their real merits.

Recession. Recession is undoubtedly the best type of operation for the purpose of weakening the action of a muscle. Jameson advocates a wide conjunctival incision in the plica semilunaris. Curdy severs the tendon with a knife. Peter (55) recommends great care in the handling of the muscle and thus condemns the use of forceps. With the aid of a hook with which he lifts the muscle first on one and then on the other side, he makes one whipstitch at each side of the tendon before it is cut. Even fanlike spreading of the tendon on the sclera seems to be of great importance for the avoidance of future cyclophoria, and the stitches should be made with proper care in order to ensure uniform attachment.

Recessions are limited by the distance to the equator of the point of attachment of the different muscles on the sclera. Thus 5 millimeters for the rectus internus, 4 millimeters for the rectus inferior, 3 millimeters for the rectus externus, and 2.5 millimeters for the rectus superior seem to be the maximum that can be receded. In the case of larger eyes (the diameter of the cornea according to Priestley Smith being possibly the best index to judge about the size of an eye), 1 to 1.5 millimeters more can be allowed for each muscle. It has been claimed that even with larger recessions no ill results such as lack of convergence have been found, and apparently with the rectus externus more liberties can be taken, but on the rectus internus the maximum limit of 6 millimeters should not be stepped over. According to Jameson a 5 millimeter recession of the rectus internus will correct 20 to 25 degrees, and the recession of the rectus externus corrects one-third of that. According to Peter (54) only 12 degrees' correction can be expected from a recession of 6 millimeters, whereas 25 degrees can be expected if the recession is combined with advancement. Results vary considerably according to individual variations of the muscles. As a rule about 5 degrees for every millimeter of recession can be estimated, if the antagonist is operated on simultaneously.

Advancement. This type of operation meant to enlarge the arc of contact is still in great favor

(Wheeler) although its results have been questioned and some controversy has arisen regarding its action. Duverger, quite some years ago, experimenting on rabbits found that after some time the advanced tendon finds itself attached to the former stump, in which case the advancement would only act through the shortening of the muscle. Prangen and Horay are of a similar opinion regarding the results of advancements, but Jameson believed that the muscular fibers are still active and can take action even when they are embodied in the attachments to the sclera. Peter is in favor of advancements because he finds that by including the capsule and the conjunctiva in the advancement about 5 to 10 degrees more can be corrected with this type of operation.

Apparently advancements will not correct more than about 15 degrees (Wheeler) except if associated with recession of the opponent. The possibility of using advancements for the purpose of correcting simultaneously vertical and lateral deviations has been considered, but an agreement does not seem to have been reached so far. The majority of papers dealing with advancement merely add details of new techniques, chiefly in the sutures. The operation lends itself to ulterior changes in the sutures for the purpose of correcting surgical defects during the first few days after the surgical procedure.

Resection. Reese's method nowadays finds great favor. The effect of the operation is that of shortening the muscle and sometimes it has been used combined with advancement in order to increase its action. Great care has been taken to make the sutures more effective and to make them safer, by attaching the muscle to the conjunctiva before it is severed. The anchorage of the suture on the tendon stump has been improved too, and several new techniques have been described to that effect. As in all operations on the external muscles, the trend now is to make a large conjunctival incision in order to be able to operate freely on the muscle.

Tucking. In order to obviate the undesirable attachments above or below the previous point of insertion a tucking operation, in which the muscle is not severed at all, was devised some time ago.

An argument raised against the tucking methods, first advocated chiefly by Burch and Grant, is that they are not very exact, as considerable stretching of the muscle fibers takes place during the first days after the operation and that consequently it is very difficult to know how much should be tucked in order to have dependable results. Possible necrosis of the muscle, due to strangulation of the blood supplying vessels, has been mentioned too. But the method has gained

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Von Blasovics described a technique for a controlled tenotomy and his method has found great favor in central Europe (Harms, 33 Miklos). Von Blasovics' controlled tenotomy is quite an improvement upon the more primitive procedure of simple tenotomy, but neither this method nor any other presented so far can compare with Jæsson's recession, the tendon of the severed muscle not being properly attached to the sclera and consequently the final attachment being somewhat uncertain and unpredictable. The favor met by controlled tenotomies can be ascribed to the possibility of subsequent improvement of the results of an operation when overcorrection or undercorrection are found to be present. This is achieved by leaving the sutures tied in a way that allows for the tightening or the loosening of the suture in the first days after the operation. More will be said about this presently.

Weakening of muscular action through other methods than tenotomies. Lengthening of muscles is seldom used any more, but occasionally the method is mentioned in the literature. Samara has recently advocated lengthening the muscle by pulling hard at it with a strabismus hook. He associates this with advancement of the antagonist. Central tenotomies are still practiced here and there but their use does not seem justified since, as it has been proved by the experiments of Watrous and Olmstead, this type of operation is effective only because the postoperative attachments to the sclera of the part of the tendon operated upon being about a reduction in the arc of contact. Peter has deliberately reduced the arc of contact by suturing the tendon to the sclera some millimeters back of the point of normal attachment. Alabaster with gold sutures pulls the muscle in the opposite direction of its action during the advancement of the antagonist, and Worth-Chavasse places a band of electrocoagulation

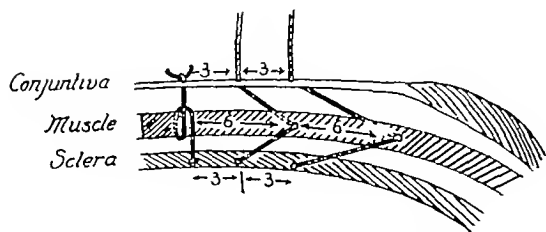


Fig 3 Diagram showing technique of the Harms controlled advancement operation

which he puts in two extra sutures through conjunctiva, muscle, and sclera and again through muscle and conjunctiva, and placed in such a way (Fig 3) that by tightening them soon after the operation it will be possible to shorten the already advanced muscle still more, thus increasing its action. Baudot described a somewhat similar method for the same purpose.

Von Blascovics, as far back as 1922, in certain cases in which slight changes in the position of the eyes (up to 5°) were still desirable, had used after operation a special dressing compelling the eye to be in extreme adduction or extreme abduction. The principle of his method was to force the eyes in a certain direction, so that the new attachments would take place in that position. Strebel and Goldman have advocated the use of that method. Instead of von Blascovics' special dressing, ordinary glasses covered with simple adhesive can serve the same purpose (Fig 4).

Methods for correcting bad operative results. Patients previously operated upon and in whom there is still some heterotropia should undergo the same careful examination as any other case of strabismus, in order to determine the proper methods of treatment at the proper time. In the case of previous recessions or tenotomies a similar operation on the antagonist is not advisable in order to avoid any degree of proptosis. For certain cases in which the ill results have been caused by unwished for adhesions between the muscles and the eyeball, Berens (11) has devised a special technique: he inserts between the adherent muscle and the sclera a transplanted piece of Tenon's capsule, taking care to turn the transplant over, so that the side which was formerly turned to the sclera, will now be turned to the muscle, thus averting the danger of renewed attachments between muscle and sclera. Capsular advancement, has been found very useful in cases of paralysis due to previous simple tenotomies.

Divergent strabismus. As a rule there are no special methods for the treatment of divergent strabismus, the same general principles mentioned

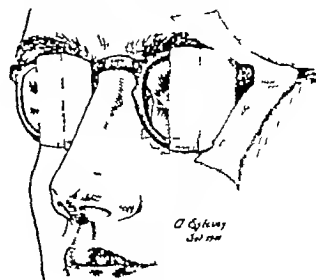


Fig 4 Von Blascovics' method for subsequent correction during the first 5 to 12 days after the operation

for convergent concomitant heterotropia begin equally prevalent. Thus an accurate diagnosis of the nature of the deviation in each case is absolutely essential so that one may choose the best method. Furthermore, recessions of the external recti will be justified only in cases in which there is normal convergence, as has been pointed out by White and Brown (80). Coppez goes so far as to recommend complete tenotomies of the external recti, an operation which he otherwise condemns. But even on the external recti, tenotomies are not very satisfactory, and if weakening of the external is desired a recession should be resorted to. Cass is in favor of bilateral advancement with resection of the recti interni. Dunnington too favors a generous strengthening of convergence through a proper operation on the interni.

White and Brown (80) emphasize the importance of vertical deviations in the success of the operative treatment in divergent strabismus, as well as in the convergent. Hypertropia should be corrected preferably before the management of lateral deviation, but in some cases, when it is impossible to discover the vertical deviation with the necessary accurateness, it is justifiable to correct the lateral deviation first. In some cases it is possible to correct both deviations, lateral and the vertical, simultaneously. Generally it is the inferior oblique which is responsible for the vertical deviation, and in such cases a tenotomy or recession (von Blascovics) of the inferior oblique is the method of choice.

Cass calls attention to the fact that operative results are very deceptive in divergent strabismus, and in many cases immediate good results are followed in a short time by a relapse. Early operation is advisable in all cases of alternating strabismus and in those in which there is improper adjustment.

Paralytic strabismus. The possibility of re-establishing binocular single vision, even if this is limited to a very small area in the field of fixation,

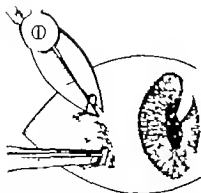


Fig. 2. Myocampter silver ring should be cut as near as possible to the conjunctiva, first where the sclera are and then where the forceps appear in the illustration. The two severed ends can then be easily removed.

much favor in spite of this, and in the hands of those who sponsor this type of surgery the results have been very good. If the tucking is performed simultaneously with a recession, there will not be so much pull on the sutures of the tucked muscle, and consequently less stretching. Apparently not more than 20 degrees can be corrected with tucking. The least that can be tucked to get any effect at all is 3 millimeters (von Blascovics).

Several changes in the technique of the tucking operation have been presented, some advocating the use of instruments (tuckers) and others, only stitches. Recently a method was described providing for an anchorage of the muscle on the sclera near the limbus (Bardansellu).

The tucking of the muscle jointly with the conjunctiva has been advocated too, in order to strengthen the operation and to render it bloodless. This has been achieved with ordinary stitches (Szymanski) or with a silver ring in the myocampter of Barraquer or Lacarrière. According to Bristow the myocampter is an improvement of Briggs' instrument presented to the Section of Ophthalmology of the American Medical Association back in 1909, and Otis Wolfe gives testimony to Briggs' priority by stating that during one of his visits to Barcelona, he showed Barraquer Briggs' instrument and that later Barraquer sent him his model. According to Wolfe Barraquer never claimed priority for this method.

Myocamptia met with considerable favor in the early thirties. Later Hubert and Lebas advocated exposing the muscle first, and then shortening it with the myocampter. This renders the method much more dependable. About 10 millimeters' shortening can correct up to 20 degrees. If recession is performed simultaneously. A Isonis in-

vestigated the pathology of muscles after myocamptia, and found the following changes in the strangulated part of the muscle: cyanosis, hemorrhages, and some necrosis and Jacques reported a case of repeated cyst-like growths on the conjunctiva over the tucked muscle after myocamptia. Removal of the silver ring about 1 month after the operation is sometimes rather difficult, as the ring is completely buried in the conjunctiva. In such cases, after the ring is uncovered each end should be held with a simple forceps and the ring should be cut apart as is shown in Figure 2 (Alvaro,).

"Cyclotomies" (O'Connor) O'Connor's clock operation was devised in 1911 and only gradually did it become extensively known. From San Francisco, where it had been used for a long time it spread gradually throughout the United States and in the last years to Europe. Everywhere it has been welcomed with marked enthusiasm. Barkan's statement about this method, calling it "the most perfect mechanical means of straightening an eye at any age" is one of the many which indicate the enthusiasm so many ophthalmologists have shown for the "shortener" operation.

The advantages of the method are chiefly the absence of sutures and of severance of the tendon. It has been pointed out by some surgeons (Wacker) that during the first days after the operation there is a rather strong reaction in the eye operated upon, but this has been denied by others (Appelman). About 10 millimeters is the maximum that can be shortened.

Smukler described a needle, $3\frac{1}{4}$ inches long, made of 14 gauge wire which he uses for winding the dermal suture round the strips of the muscle. He uses special grooved books to keep the strips separated for the insertion of the suture. The muscle is dissected as far as the equator and the dermal sutures should be placed at a certain distance from the point of attachment in order to prevent too much pull on the muscle fibers. Not more than 8 dermal sutures should be used. Cementing both ends of the dermal suture bundle with a special metallic cement is a method advocated by both O'Connor and by Smukler. The sutures should be left for about 2 weeks.

Methods for correcting after effects Apart from the controlled tenotomies, which lend themselves to further changes in the position of the eye a few days after the operation by tightening or loosening the suture, some methods have been devised of late to enable the surgeon to perform an after correction, if the results do not seem to be satisfactory in the first few days after operation. Hains (13) describes a new method of advancement in

upper part of the field of fixation—where there had been only a small vertical deviation, or none at all before the operation—there will be an overcorrection in the sense of a contrary vertical deviation. In the lateral movements results are still worse as the vertical position of the paralyzed eye is dependent upon the oblique muscles, when the patient looks toward the healthy side, the vertical deviation increases in proportion to the increased turning of the paralyzed eye, and conversely decreases when the patient looks away because the vertical position of the averted eyes is influenced by the vertical recti. After recession of the superior rectus there would be an increased deviation both in adduction and in abduction. Still more unsatisfactory is the effect of the recession of the superior rectus on the rotation of the eyes. Both the superior oblique and the superior rectus rotate inward, and consequently weakening of the superior rectus will increase the disclination. Advancing the inferior oblique (advocated by Landolt) would likewise cause a more pronounced disclination, and would improve parallelism only in the lower part of the field, but not in the center, as this muscle is inadequate in the nasal quadrant of the lower half of the field of fixation.

Best results show recession of the inferior rectus of the contralateral eye. This equalizes the function of the associated depressor muscles in the two eyes. If a tenotomy is performed there may be an overcorrection in looking down, but a recession can graduate the weakening of the inferior rectus so that no such results will ensue. It should be remembered that the left superior oblique and the right inferior rectus are associated in depressing and turning the eyes to the right. The left superior rectus turns the upper part of the cornea toward the right of the patient (internal rotation) and the right inferior rectus turns the upper part of the cornea to the right too (external rotation). If the left superior oblique is paretic the upper part of the cornea in the left eye will move to the left (outward). By receding the inferior rectus of the right eye the muscle is weakened and consequently the upper part of the cornea will be turned to the left (inward). Thus the vertical lateral and rotating elements will have been corrected.

Paralysis of the rectus internus References to surgical treatment of paralysis of the adducting rectus are rather scanty in the literature. Shortening of the rectus internus and simultaneous recession of the rectus externus are generally advocated. Both Jackson and Peter (54) dissect the internal halves of the superior and inferior recti and transplant them to the point of insertion of

the rectus internus. Several cases have been reported, mentioning good results, of the transplantation of the superior oblique to the point of attachment of the rectus internus (Wegener), shortening of the rectus internus and recession of the antagonist being performed at the same time.

Paralysis of the rectus superior An advancement or shortening of the superior rectus has been advocated. O'Connor's cinch operation after tenotomy of contralateral inferior oblique, if this proves insufficient, has been used for that purpose. Peter advances the rectus superior and transplants the upper halves of the tendons of the rectus externus and rectus internus to the new point of attachment of the superior rectus. An advancement attaching the tendon a few millimeters temporal to its previous attachment has been mentioned by Peter too (54). When there is an overaction of the inferior oblique of the contralateral eye, this muscle should be operated on, either by receding it, according to Rugg Gunn's method, whereby it is reattached to the periosteum about 6 millimeters from its normal insertion, or by a simple tenotomy.

White (77) favors a careful myotomy of the inferior oblique of the contralateral eye and, if this proves insufficient (Gifford, 27), an advancement and resection of the paralyzed muscle. In cases in which even the combination of these two methods is not able to correct the deviation, a recession of the rectus inferior on the paralytic eye should be resorted to. Both Dunnington and White (79) agree about the choice method being either the advancement of the rectus superior or a tenotomy of the inferior oblique of the contralateral eye. When the paralytic eye is used for fixation, there is an overaction of the synergical muscle of the other eye, and tenotomy of the contralateral inferior oblique is to be favored, and, conversely, when the good eye is used for fixation and no such overaction exists, an advancement of the paralyzed superior rectus should be performed. Operations on the superior rectus have the disadvantage of causing a disturbance of the movements of the upper lid and diplopia in the lower field of fixation.

Paralysis of the rectus inferior An advancement with resection of the paralyzed muscle seems to be the method of choice. If there is an overaction of the superior oblique, a recession of the trochlear of the contralateral eye has been suggested (Berens), and if there is a spasm of the direct antagonist, a recession of the superior rectus. Wiener suggested severing the inferior oblique close to the sclera, reattaching it nasalward from the attachment of the inferior rectus. Casten



Fig. 5. Gutzert's muscle speculum.

is welcomed as a blessing by the majority of patients. This fact, recently emphasized by Gifford (27) shows the importance of the surgical treatment of paralytic strabismus. The knowledge of conditions of binocular vision before the onset of paralysis is essential for the choice of the surgical method in each case, and the use of prisms after the operation in order to correct small defects and enable simultaneous macular perception is of equal importance.

An accurate diagnosis of the nature of each paralysis, including a minute investigation of the functional condition of each muscle and of the synergic action of all muscles involved in the movement of the eyes in the several directions in the field of fixation, is of paramount importance for the choice of the surgical method in each case. According to Bielschowsky especially in the case of vertical deviations, the following questions must be answered before a decision is made as to if and how any kind of paralytic strabismus may be surgically corrected: (1) Does the vertical deviation increase in looking up, or in looking down? (2) Is it different in the right and left halves of the field of fixation? (3) Are the double images of contours parallel in the whole field of fixation, or only in a certain part, being inclined toward each other in the other part? (4) Does the tilting of the head around the sagittal axis without changing the direction of the visual lines influence the magnitude of the vertical and the meridional deviation, and, if so, in what manner? The answers to these questions will enable one not only to differentiate between a true paralytic strabismus and a nonparalytic heterophoria but also to discover which muscles are involved—whether those which are paralyzed or those which have developed an overaction due to secondary contracture.

The surgical treatment of paralytic strabismus should be resorted to only after 6 months have elapsed after the inception of the paralysis with-

out any signs of recovery (Bielschowsky), but afterward early treatment is advisable in order to avoid contractures of the antagonist.

The operative treatment should be directed, whenever possible toward increasing the efficiency of the paralyzed muscle as it should be remembered that, according to Sberington's demonstration in 1893, the lengthening of an antagonistic muscle under normal conditions should not be regarded as a passive stretching produced by the contraction of the agonist, but is really due to an active relaxation that takes place even if the agonist does not function at all. It is now recognized therefore, that it is not possible to improve the function of a paralyzed ocular muscle by means of weakening its antagonist alone. On the other hand, Landolt's assumption that when shortening of the paralyzed muscle proved inefficient the contralateral homonymous status of the shortened muscle in one eye should be strengthened too, does not stand good any more in cases of long standing paralytic deviation with secondary contractions. Landolt very rightly opposed tenotomies and that is possibly the explanation for his policy. Recessions, however not bringing about the poor results of simple tenotomies, enable us to increase the effect of the shortening operation on the paralytic muscle by relaxation of the pull of the antagonist. In some types of paralytic strabismus strengthening of the paralyzed muscle is technically difficult and weakening of the direct antagonist is not enough or may even have a somewhat unexpected result, due to an overaction of contralateral muscles of synergical action to the paralyzed muscle.

Especially in cases of paretic vertical muscles there are other factors to be taken into consideration whenever parallelism of the eyes is to be re-established in the largest possible area of the field of fixation by means of an operation. Thus not only the overaction of the contralateral associate has to be considered as moving the eye vertically but its adduction or abduction and especially its conformation or declination are of great importance.

As an example of the complexity of matters regarding paretic vertical muscles Bielschowsky discusses the subject of inveterate trochlear palsy. As the strengthening of the paretic muscle is difficult, there might be a possibility of improvement of the vertical deviation by the weakening of the rectus superior of the paretic eye. But this would be only in a very limited area of the field of fixation, the effect of this operation being less in the lower part of the field—where the vertical defect had been greater before—whereas in the

The method advocated by Landolt, of advancing the inferior rectus, has been equally abandoned. Wheeler devised an operation to shorten the paralyzed superior oblique, but its technique seems rather difficult and its use has been discouraged (Peter, 54). Auran dissection strips of the external and inferior recti and attached them to the sclera at a distance of 3 millimeters from the limbus at the 7 30 meridian.

Paralysis of the inferior oblique An advancement operation for the inferior oblique has been described by Wheeler. The muscle is detached from the orbit, pulled out, and sutured to the cheek bone. Recession of the superior rectus of the contralateral eye has been advocated by White and Berens.

Bilateral paralysis of homonymous muscles Handling of bilateral paralysis of homonymous muscles is rather difficult. According to what has been published so far (White, 78), bilateral paralysis of the rectus superior, when it is predominant in one eye, calls for tenotomy of the inferior oblique on the less paretic eye, and according to the result shortening of the superior rectus of the lower eye or tenotomy of the inferior oblique of the other eye. When the patient uses constantly only one eye for fixation (generally it is the more paretic eye), the external rectus of the deviated eye should be operated on by performing an advancement or recession according to the lateral deviation in each case and a tenotomy of the inferior oblique. When one or the other eye is alternately used, bilateral tenotomy of the inferior obliques and in mild cases bilateral shortening of the superior recti should be performed. Whenever bilateral paralysis of the superior recti is almost complete, care should be taken not to touch the inferior obliques, in order not to weaken the elevators entirely.

For bilateral trochlear paralysis Jaensch prescribes recession of the inferior rectus on one eye followed by a similar recession on the other eye if necessary, the second operation depending upon the results obtained in the first.

ANESTHESIA

As in other branches of surgery, the latest developments of anesthesia have done much toward improvement of surgical treatment. Possibly the favor enjoyed by the simpler and cruder methods, the results of which were so unsatisfactory, was chiefly due to the lack of proper methods of anesthesia. There is no doubt about the influence of anesthesia on the opinion of many ophthalmologists as to the minimum age at which to operate on a child with strabismus. General anesthesia

was not favored in the older days because during the operation the deviation could not be seen, it was claimed, and consequently the surgeon had nothing to gauge the operation by. Lately however, as has been pointed out by Dunnington, accurate preoperative examination of the patient permits establishing a definite plan beforehand.

Peter (55) favors general anesthesia in all cases, as he believes that local anesthesia is always responsible for some degree of edema which may cause important landmarks to become obscured. Anyway for children under 12 and for those adults whose temperament or disposition prevent them from being co-operative with the operator, general anesthesia is essential.

For general anesthesia the use of ether, vinylene, diethyl ether, nitrogen peroxide, ethylene, cyclopropane (the two latter are inflammable) has been advocated. Magill's tracheal tube should always be used in order to keep the operative field unobtruded (Prangen, 58). Morphine sulfate 0.01 gram and atropine sulfate 0.0004 gram hypodermically, should be given about 30 minutes before general anesthesia.

Evipal, pentothal, and avertin are very useful too, but in most instances a small amount of ether will have to be added. Barbiturates are generally used as preoperative sedatives the night before, and on the morning of the operation both for general and for local anesthesia.

When local anesthesia is used, instillation of anesthetic drops, the gauze pack (Meller), and injection into the muscle sheaths will be found insufficient, and block anesthesia will have to be resorted to. But as it has been pointed out (Weill, Bressler) local anesthesia is unsatisfactory in many cases, especially in the case of undue traction of the muscles and tendons with the hook. The combination of local and general anesthesia has been favored too, with the purpose of reducing the amount of general anesthetic which will be necessary for the operation.

INSTRUMENTS

Many instruments have been built for the particular purpose of rendering one or more phases of a certain type of operation easier, and each operator becomes attached to the type of instruments he is used to. Lately new instruments have been perfected, and the use of others introduced. Thus, Spaeth (65) emphasizes the importance of the lids of the speculum covering the cilia to prevent tiny clippings falling into the wound. For the same purpose Durr uses a sterile rubber sheet in which he makes a slit to insert the speculum, the rubber tissue covering the eyelashes completely.

reported good results in a case of congenital absence of the inferior rectus, after having transplanted the external rectus to a spot midway between its former attachment and the insertion of the inferior rectus. Extension and depression of the eyeball were thereby achieved. Casten advocated simultaneous tenotomy of the inferior oblique if found necessary. Peter advocated the advancement of the inferior rectus attaching it a few millimeters temporward (and obviously nearer to the limbus) from its former attachment. Barrels, in a case of absence of the inferior rectus and fibrous band of the superior rectus, tenotomized the latter and pulled the eye down with sutures on the limbal conjunctiva tied on the skin of the lower lid.

Paralysis of the rectus externus. This appears to be one of the most common kinds of paralytic strabismus. Advancement or shortening of the external rectus and recessions of the internal rectus have been advocated.

A simple tenotomy of the internal rectus combined with special stitches meant to pull the eye toward abduction has been described by Vogt. The Hummelshelm type of operation with several improvements in its technique has been favored lately by Gifford (28) Belsae Goodman, Lancaster, Alvaro (1) and several others, with fairly good results. Gifford reports abductions of 5 to 35 degrees after the operation. O'Connor instead of using the external halves of the superior and inferior recti, transplants the internal halves. Wiener prefers to sever the rectus externus 15 millimeters from the sclera, split the scleral part in two horizontal halves, and transplant the superior and inferior to the superior and inferior recti.

There is some controversy regarding the way in which the Hummelshelm type of operation works. Some as Bielachowsky and White (79) believe that results are due mostly to the recession of the overactive rectus internus and White is rather conservative about disturbing the vertical balance although Gifford (7) has never noticed any change in vertical balance after operations of this type. Spaeth (64) mentioned the results of experimental work done at the Graduate Hospital in Philadelphia according to which the action of the muscular slips is merely that of stays, thus permitting the tension of the other abductor muscles to act whenever reciprocal relaxation of the abductors occurs. Meyer using indiscriminately the nasal or temporal strips of the superior and inferior recti, stresses the importance of careful dissection in order to prevent too much pull on the sutures. Worth-Chavasse still favors bilateral

recession of the internal recti, but that method does not seem to be favored by the majority any longer. Apple calls attention to the fibrous tracts appearing under the contracted internal rectus, which have to be severed in order to get good results.

Paralysis of the superior oblique. Next to abducens paralysis this is the most common of ocular muscle paralysis. Bielachowsky calls attention to the fact that trochlear paralysis has become more common in the last 30 years and explains this by the more frequent operations of the Killion type in which the trochlea is easily loosened. Paralysis of the superior oblique causes some form of torticollis, and therefore an early operation is advisable especially in children.

Von Graefe and Alfred Graefe quite a long time ago had devised a surgical treatment for trochlear paralysis which was abandoned for many years and has now found general favor again, namely tenotomy (now substituted by recession) of the inferior rectus of the contralateral eye. With this method, as it was recently mentioned by Berens, Dunnington, McMillen, White, Argassius, Marx, and Plocus, results are quite good, although because the patient looks down, the paretic eye is too high, and conversely too low when the patient looks down and away as it was mentioned recently by Messmann. Recession of the inferior recti has the disadvantage in many cases of causing a certain degree of ptosis of the lower lid. In order to prevent this, a careful suture of the conjunctival wound is essential. Bielachowsky prefers not to tie the sutures of the receded tendon, in order to be able to tighten or loosen them according to results obtained in the next few days.

Tenotomy of the inferior oblique of the same eye is favored too (Homan) and, according to Spaeth, Duane and Bielachowsky. It should be used chiefly when there is an associated exophoria. The method formerly described of recession of the inferior rectus of the contralateral eye, is the method of choice when there is esophoria. White favors operating on the contralateral inferior rectus first, and then, if necessary, on the inferior oblique. Gifford, on the other hand, prefers to operate on the inferior oblique first. Dunnington, Messmann, Borsotti, and others favor tenotomy of the inferior oblique only when there is a strong secondary contracture.

Johnson a method of transplantation of the superior rectus was recently favored by Vaquero Barriere and Savin still favors the method, now generally abandoned of recession of the superior rectus.

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For measurements of the number of millimeters in advancement, shortening resection or recession operations, Berens built a special caliper on which the distance between the two points is easily readable, and Green described another model one point of which is very thin and guarded in order to enable easy fixation with little traumatism and no danger of perforation the other blade-like end of the instrument being meant for marking the sclera with gentian violet or fuchsin.

Tendon spreaders taking the place of the two books to be held by an assistant were built by Wursch in Berlin and by Grisehaber in Switzerland after the patterns of Streiff and Schweligger-Gutzelt respectively. Similar to these tendon speculums is the bodkin described by Lodge made of thicker stainless steel wire. The handle and the hook with its terminal eye are ground to the original gauge but the middle third is forged into a grooved director curved on the flat. The bodkin is meant to put the extraocular muscle at rest and render it more accessible to sutures.

SUTURES

A rather large number of methods for the operative treatment of strabismus have been devised just because the existing sutures were found to be unsatisfactory. Lancaster back in 1901 showed, by his experimental work, exactly how much tension was necessary to pull the simple sutures which were used in those days through the muscle fibers, and the results were not very encouraging. Since then several more reliable types of sutures have been described such as the stitches zigzagging through the muscle (Lancaster-Thompson), Ziegler's "whipstitch," and the mattress suture.

By means of a double armed thread a great number of suture may be made with but one thread according to Jameson all other things being equal it is best to be able to bring about the apposition of all the tissues with one single suture. Fanlike spreading of the tendon on the sclera, however, is essential, and care must be taken that the sutures keep the tendon in proper position. Strangulation of all the muscular fibers should be avoided by all means, and for that purpose the central part of the muscle should be left free of sutures (Lancaster). The violation of this principle is responsible for many bad results, which change a tucking operation into a tenotomy the adhesions of the muscle and the capsule to the sclera at a point where the sutures rest on the sclera, being responsible for a less catastrophic result and for the still disappointing *status quo* (Spaeth 63). The careful handling of the muscles is just as necessary and forceps should be

applied only on those parts which are intended for resection.

The fact that silk could be used without any misgivings in buried sutures (Lancaster) made silk sutures more and more popular in the early thirties. Lately however, improvements in catgut, rendering it more reliable as to sterility and endurance (10 or more days without resorption and causing little reaction) and the appearance of atraumatic needles have turned the tide so that today catgut is gaining more in favor. Generally No. 000 catgut is used for resections and advancements and No. 00000 for recession and conjunctival sutures (Prunigen, 58).

According to Muegge silk should be waxed before it is used (7 parts of yellow beeswax, 1 part of almond oil, 1 part of salicylic acid—Peter, 55). For advancements on the lateral muscles twisted silk No. 4 or braided silk No. 1 should be used, for the vertical recti, twisted silk No. 2 and for conjunctival sutures, twisted silk No. 1 (Peter 55).

Scleral sutures have become commonplace, and scleral perforations formerly a formidable occurrence are really rare (Butler).

SUMMARY AND CONCLUSIONS

The large number of operative methods and the almost infinite variations of sutures are an indication that, as it has been stated by C. Maynard Wheeler "There is no unanimity of opinion as to the proper handling of strabismus. Comparably favorable end-results can be achieved by several methods. The procedure of choice for any surgeon is the one with which he is most familiar and in the performance of which he is most skillful, provided of course the right type of operation for each case has been carefully chosen.

Regarding immediate postoperative dressing there appears to be some slight individual variation. Binocular occlusion for at least 1 to 7 days is almost generally accepted. Barraquer's occlusion bandage seems to be most comfortable to the patient.

Complications are rare. Butler in 30 years lost only one eye, due to panophthalmitis, because of infected catgut, and Kiehle and Henton in 156 operative cases had only one eye complicated with uveitis. Against local reactions, foreign protein has been advocated (Spaeth, 64) and recently sulfanilamide has given good results when administered orally and locally. The local use is conditioned by its solubility so that enough concentrated solutions can be used. For that purpose sodium-sulfanilacetylthylamide of which 30 per cent solutions can be easily obtained shows good results.

DEFENSE NEEDS SUGGEST TIMELINESS OF COLLEGE PROGRAM FOR GRADUATE TRAINING IN SURGERY

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At the third Annual Conference of the American College of Surgeons, a special committee under the leadership of the president of the College, its members will represent high medical education as well as professional practice in the profession. That purpose, therefore, of the conference will be to discuss the problem of the college and to develop a plan and program of graduate training in surgery in the developing college. Adjustment and enlargement of its present program to meet the current needs have seemed for this committee its present major responsibility in directing the advancement of the college and surgery as a specialty through the standards of scientific education and practice.

At the present time, the college has experienced the "outward" and "inward" expansion tendency of the College in the program of graduate training in surgery. It has developed quite naturally in connection with Hospital Study Division. The stimulation that it is giving to the creation of more opportunities in approved hospitals for surgical education is helping to secure our military forces today of surgical service of high quality. It is also aiding our general population to continue having adequate service in civilian hospitals notwithstanding the enlistment of many surgeons in the Army and the Navy. The need for national defense, that includes health defense as a primary requisite, suggests the timeliness of increased effort by the College to provide additional opportunities for adequate training in surgery.

Interruption of training due to enlistment in military service is a problem that existing conditions present. We can ill afford to curtail training for surgery at a time when we urgently need more and better trained surgeons. As a partial solution, certain of the larger general hospitals of the Army and the Navy will probably arrange to provide opportunities for certain junior medical officers to continue their training in these institutions when it is interrupted by enlistment. For those exceptionally well qualified whose training could not be pursued in military hospitals, perhaps exprop-

Chairman of the Committee on Graduate Training in Surgery

tion or deferment from military service will be obtained. It was the consensus of the Committee on Graduate Training in Surgery held during the last Annual Conference that in the ensuing year considerable effort should be devoted to the formulation of a definite plan for the solution of the problem. Each recent graduate of medicine has now completed his internship and now having an opportunity to be put approved for graduate training in surgery should be permitted to continue his training, if possible, without interruption. The American College of Surgeons can advise the War and Navy Departments that thousands of service to hospital patients are also available when the institution utilizes its resources for professional education. The atmosphere immediately becomes more scientific and more progressive and this reacts to the good of the patient. Difficulties encountered in providing advanced study of the basic medical sciences and research will no doubt be surmounted with the cooperation which may be expected of the medical schools and civilian hospitals. However, the needs of our military forces must be met and under the present world conditions some of our most desirable and ambitious plans may have to be changed.

As for the status of the program in general, it was announced at the 1941 Congress that 216 hospitals, 16 more than the previous year have acceptable programs for training in general surgery and/or the surgical specialties. Undergraduate teaching is being done in 143 of these approved hospitals. Connections with a medical school provide certain phases of the graduate teaching program in 158 of the institutions approved. Of particular interest is the fact that 31 hospitals without medical school connections are now utilizing their own facilities sufficiently to be included on the approved list. The College recognizes the educational opportunities existing in certain group clinics. Eight of these organizations are included in the present approved list and more are expected to be added from time to time as they develop sufficiently comprehensive programs. As proof that opportunities may be created in different types of hospitals, the 1941 report shows that 109 of the hospitals approved

the standards of the practice of surgery which is promoted by the holding of a Forum on Fundamental Surgical Problems in connection with each Clinical Congress. Those who conceived and developed this idea which proved such a popular feature of the Boston meeting are to be congratulated and there is every reason for its repetition. This creation of opportunities to communicate the results of research will focus more interest on the basic science and research aspects of the graduate training program of the College.

In the October 1941 issue of the College Bulletin there were published revised and additional descriptions of approved plans for graduate training in general surgery and the surgical specialties. It was felt that the republication of these plans was justified by the changes wrought in the preceding year and by the intensification of interest in surgical training as a result of the national defense effort. The up-to-date published outlines of these educational programs provide information for the medical student and intern and also an easy method of comparison between institutions. If thereby a wholesome spirit of rivalry is engendered which will lead to the improvement of some of the plans and the inauguration of additional ones, one of the primary purposes of republication will have been accomplished.

The national emergency is placing obvious difficulties in the way of progress, but despite these difficulties the prospects are good for making 1942 significant year in the annals of surgical education. It is fortunate that the graduate training program is already so far advanced that it can prove its benefits in these critical times when the country is dependent to a greater extent than ever before upon competent surgeons for both military and civilian service.

assistant was in military service. They reported that the obtaining of adequate medical records was seriously affected by the shortage of internes and residents, and that maintaining adequate nursing service was threatened by the decrease in nursing personnel in many hospitals.

These conditions have interfered considerably in carrying out some of the requirements of Hospital Standardization, but field representatives found that in most instances adjustments were being made to continue to meet the standards. On the whole the performance was remarkably good and augurs well for a creditable war time record. The incentive supplied by the desire for approval by the College promises to be exceedingly helpful in maintaining the quality of hospital service. Administrators say that the public is becoming better informed on ratings of hospitals, and prospective patients frequently ask whether the hospitals in their community are approved. A further factor spurring hospitals to seek and hold approval is the stipulation by many agencies that patronage or aid go only to approved institutions. This is true of state county and city governments which subsidize hospitals for the care of indigent patients of group hospital service plans of chambers of commerce in endorsing campaigns for funds by local hospitals, of insurance companies when they grant reduced rates on liability insurance of banks and finance companies in making loans to hospitals of state boards of nursing education in accrediting schools of nursing of hospitals accepting affiliate students for special courses in nursing of the American Red Cross in its extension program of volunteer workers and of federal and state governmental departments charged with the granting of funds for indigent crippled children's care. It will doubtless also apply to aid extended by the federal government for financing additions to physical plants and for meeting the expense of training certain types of personnel. All of these agencies show by their use of it that the gauge of approval is a valued help to them in determining which hospitals merit their assistance.

In the first World War the War Department lacked reliable means of judging the competence of physicians, particularly specialists consequently many men were misplaced—as one surgeon expressed it, there were numerous round pegs in square holes. Now that hospitals are standardized, and their medical staffs are organ-

ized, it should be possible to ascertain directly from his hospital what standing the individual physician has in medicine, surgery or a specialty. The College and other medical organizations also now have complete information concerning their members. It is essential that during the period the requirements of the College concerning appointments to, and organization and control of, the medical staff be met as usual, with a minimum of tolerance of practice outside the designated field in case of necessity only.

An interesting feature of the 1941 Hospital Standardization Conference was a series of panel discussions on the obstetrical department, the department of orthopedic surgery the department of anasthesia, the department of ophthalmology and otolaryngology and the department of urology respectively. The discussion covered the essentials pertaining to efficient operation of these departments, and included consideration of education and training of the various specialists.

The 1941 list of approved hospitals, as announced at the Hospital Standardization Conference showed 2,526 institutions fully approved, 347 provisionally approved, a total of 2,873. The total number of hospitals under survey in 1941 was 3,688, of which 77.9 per cent were approved. With the country at war, it is especially encouraging to have so many military and civilian hospitals which are organized and equipped to afford the physician the greatest possible assistance in his endeavor to save life and minimize suffering and disability from illness and injury. This year it is planned to promote the standardization of those Army hospitals which have not been approved, owing to the fact that it has not yet been possible to survey them. Last fall in continental United States there were 218 Army hospitals with a total bed capacity of 79,019, which is rapidly growing.

The need now is to view our hospital situation as a whole, with due consideration for safeguarding both military personnel and civilians. We face total war which means total hospital service. Our 24 years work in active encouragement of the improvement of hospitals is yielding high returns today in preparedness to meet the needs of America at war. Unrelaxing effort to keep the standards high will bring us through the conflict with a brilliant record of service by our great modern hospitals and the personnel that they have trained.

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The Thirty-second Annual Clinical Congress
 of the American College of Surgeons will be held
 in Chicago, October 19-23, 1942

CLINICAL CONGRESS TECHNICAL EXHIBITION

LEADING manufacturers of and dealers in surgical instruments, hospital apparatus and supplies, diagnostic and therapeutic apparatus, pharmaceuticals, and publishers of medical and surgical books were represented in the Technical Exhibition at the Hotel Statler in Boston, November 5-7 1941

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SURGERY

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THE SUPERIORITY OF FINE CATGUT OVER FINE SILK AS A MUCOSAL SUTURE IN GASTRIC SURGERY

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WHILE investigating the tissue reaction of various suture materials in abdominal surgery performed on animals, we were impressed by an outstanding and constant feature the sloughing of silk through the gastric mucosa when this material was used in surgery of the stomach. This was indicated by the presence of long, redundant, intraluminal loops of silk with areas of necrosis at their points of entrance and exit, as well as between them. Further, the presence of these loops has been noted gastroscopically by Schindler, as well as by us, in humans after gastric surgery in which silk was used as the suture material. In all instances when fine catgut was used, there was a minimal mucosal reaction and at no time were loose strands noted in the gastric lumen.

SUTURE MATERIALS

The argument concerning the use of catgut or silk for ligatures and wound closure has continued since 1869 when Lister noted a localized collection of cloudy fluid about a silk ligature which had been used for ligation of an aneurysm 10 months before. Kocher (7, 8) and Halsted, in the early days of aseptic

surgery, and Howes (4), Howes, Sooy and Harvey (6), Whipple, Elkins, in recent years, have championed the cause of silk.

Halsted stated

"Let the surgeon interested in making the comparison, take a running subcuticular stitch on the one side with catgut, on the other side with fine silk (No. A or AA) and observe the healing wounds from day to day. There is not only greater local reaction in the cases sewed with catgut, but in them the wounds will occasionally open at one or more points to discharge a few drops of clear or cloudy fluid."

It is noteworthy that Halsted did not mention the size of catgut. At that time (1913), Nos. 1, 2, and 3 catgut were the sizes most generally used, and, in 1914, Phillips speaks of No. 00 as the smallest size. In fact, No. 000 catgut which corresponds in size to No. A silk was not available until several years later. The present fine gauge catgut, including No. 0000 and No. 00000 which have diameters closely approximating that of No. AA silk, was placed on the market only in recent years. Therefore, Halsted's comparison was not a fair one, because in his time he did not have available sizes of catgut sutures as fine as the sizes of silk which he was using. It seems obvious that Halsted's superior results with fine silk as compared with those which he obtained with catgut were due to the fact that he used much smaller sizes of silk which, in

From the Foundation for Clinical and Surgical Research and from the Department of Surgery and Laboratories of the Philadelphia General Hospital



Figs. 1 and 2, above—two days
Figs. 3 and 4, below—seven days

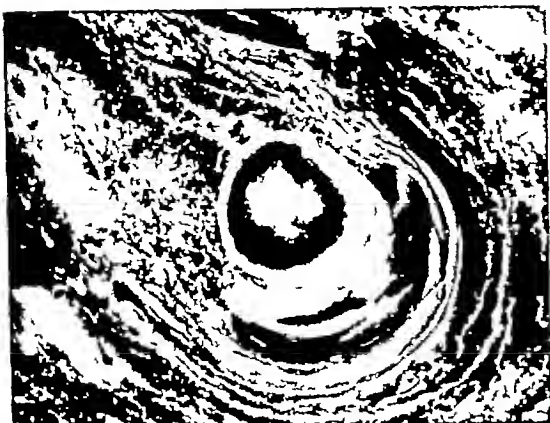


Fig 9

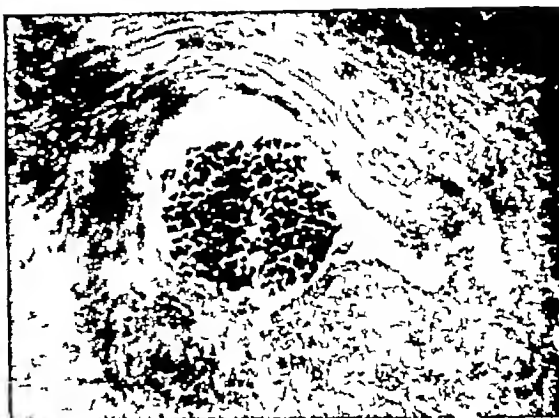


Fig 10



Fig 11



Fig 12

95 per cent) resorption of the petechial hemorrhages. One redundant loop is present, probably due to poor technique in the operation, because the mucosa is perfectly clean and healthy at the point of entrance and exit of the loop. In the silk specimen much of the traumatic hemorrhage is still present and 4 loops with early redundancy are seen. The wound shows more edema.

Four days. In the catgut specimen, the wound is clean with little evidence of edema or petechial hemorrhage. The silk wound has much edema, petechial hemorrhage, and many long redundant loops with evidence of mucosal sloughing from pressure necrosis at their points of entrance and exit.

Five days. The No 00000 wound is perfectly clean with four small redundant loops

whose points of entrance and exit show no evidence of necrosis. The No 0000 silk wound shows much delayed healing, delayed petechial resorption, much edema, 12 redundant loops with surrounding tissue necrosis.

Seven days. The catgut wound is perfectly healed with almost no evidence of the suture line in 60 per cent of its circumference (Fig 3). The silk wound is fairly clean with a few areas of necrosis still present but edema still notable. Many long redundant loops are present, undoubtedly these must have sloughed through their original entrance areas to have become so long (Fig 4).

Ten days. The catgut wound is healed—perfectly clean (Fig 5). The silk wound still shows areas of necrosis along the suture line, and redundant loops are present (Fig 6).

themselves, tended to provoke less of a foreign body reaction. Further the use of larger needles with larger sutures produces greater trauma and dead space which add to the insult to the tissues and invoke heavier leukocytic response.

We have repeatedly observed that tissue reaction to catgut is proportional to the size of the suture. When fine catgut is used, there is less tissue trauma from the suture itself and from its transit. Apposition is more nearly perfect since more stitches may be placed in given space lessening the possibility of dead space. These observations have been reported by Bower Burns and Mengle.

EXPERIMENTAL INVESTIGATIONS

In order to evaluate our observations concerning the behavior of catgut and silk as mucosal sutures, the following experiments were carried out.

Operation. A vertical bisection of the stomach of each of 14 dogs was made and the continuity of the organ re-established by using two rows of continuous sutures. The operating team used the identical technique on each dog. All animals had been on the same diet for 1 week and each weighed approximately 12 kilograms. Under morphine and atropine sedation and open drop ether anesthetic technique being used, an upper left incision was made. Bisection was accomplished by making a line drawn from the anastomosis of the left and right gastric arteries on the lesser curvature to the anastomosis of the left and right gastropiploic arteries on the greater curvature. The lesser peritoneal cavity was entered by ligating the gastropiploic vessels approximately 1 centimeter to either side of the elective site. The stomach was then gently pulled down and ligation was performed on the gastric arteries of the lesser curvature, 1 centimeter to either side of the proposed bisection site. In this manner a minimal and constant diversion of blood flow was induced. The stomach was divided between two straight rubber clamps with fine right scissors. The bisection was closed with two layers of continuous, running sutures of catgut or silk in the posterior and anterior wall. The first suture line included the

serosa and muscularis, while the second included the mucosa and submucosa. Then the clamps were removed and the abdomen was closed in layers with continuous linen sutures. Animals were operated on in pairs; chromic catgut was used for the stomach sutures in one and black silk in the other of each pair.

Suture material. In order to eliminate the size of the suture as a possible factor in causing tissue reaction we decided to employ identical sizes of absorbable and nonabsorbable suture materials. We selected No. 0000 black silk which gauged 0.006 inch in diameter because this size corresponds to No. AA silk as used by Halsted. For the absorbable suture we chose medium chromic catgut having an average diameter of 0.006 inch which thus was the equivalent in bulk of the silk. This suture material is designated No. 00000 catgut.

The No. 00000 chromic catgut was more easily handled. It has more body than silk and does not cling to gloves or tissues. However the No. 00000 silk presented no real difficulty. Neither suture broke at any time during the experiments.

Postoperative care. The postoperative management was the same in all cases: small amounts of water on the second day, milk on the third day, milk and bread the fourth day, and unrestricted diet on the fifth day. All animals recovered and all wounds healed by primary intention.

Pathological specimens. Stomach specimens of each series were taken at 3, 4, 5, 7, 10, and 14 day intervals. Colored photographs of the mucosal suture lines were made in each instance within an hour. Histological sections were made of each specimen.

Gross appearance. Two days. Both specimens show the same amount of traumatic petechial hemorrhage along the suture line due to the use of forceps and the needle transit. The No. 00000 catgut line is cleaner (Fig. 1). The No. 00000 silk shows two necrotic areas, one 0.5 centimeter and one 0.8 centimeter in length in the lower half of the specimen. In 6 areas, beginning redundancy of the silk loops is present due to sloughing through the mucosa (Fig. 2).

Three days. No. 00000 presents a very clean wound with almost complete (at least

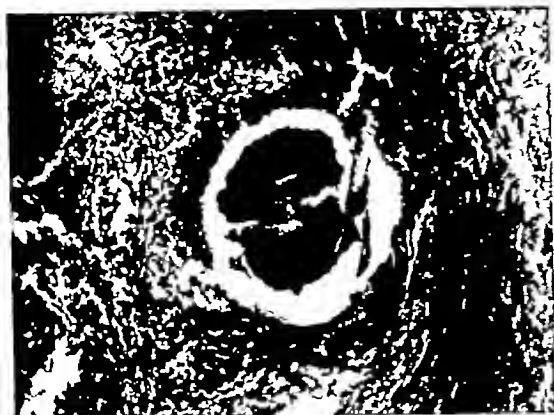


Fig 13

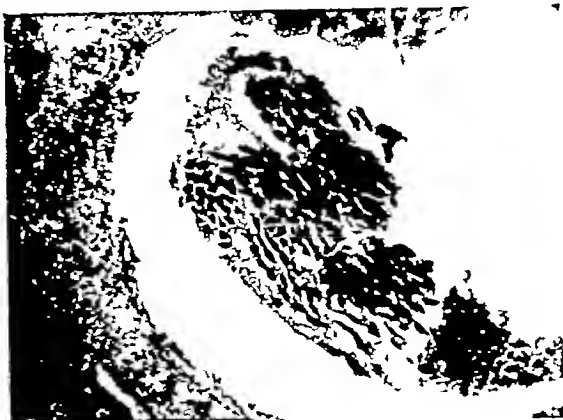


Fig 14



Fig 15

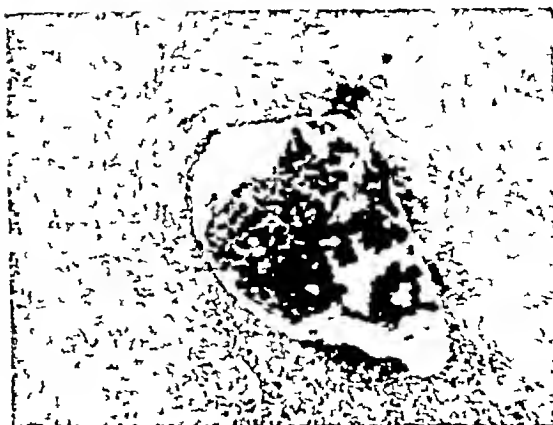


Fig 16

Certain it is that the use of a continuous mucosal suture of silk stands contradictory to some of Halsted's five tenets first stressed in 1913

"(1) Use transfixion ligature, as finer material can be used by such a method, (2) use silk not coarser than No C, (3) use interrupted sutures, (4) use a greater number of fine stitches rather than a few coarse ones, and (5) avoid the combined use of silk and catgut"

Moreover, Halsted emphasized the use of silk in clean wounds, which is an impossibility in the alimentary mucous membrane

We have demonstrated that, when fine silk sutures are used, gross tissue necrosis is present in the mucous membrane long after the healing process has subsided in the wounds sutured with fine chromic catgut. It

is obvious, therefore, that there is more danger of intramural infection from the contaminating contents of the gastrointestinal tract when silk is used. The ideal suture material for the mucous membrane is one that seals it as quickly as possible and permits it to remain sealed. Bower, Burns, and Mengle showed that divided capillaries inosculate as early as 4 days after suture of previously divided gastric mucous membrane of young dogs. Absorbable fine chromic catgut is superior to nonabsorbable fine silk in this respect.

CONCLUSIONS

1. Fine chromic catgut is more easily handled than silk of the same caliber.

2. The tissue reaction to fine silk in the mucosa resembles the reaction toward a

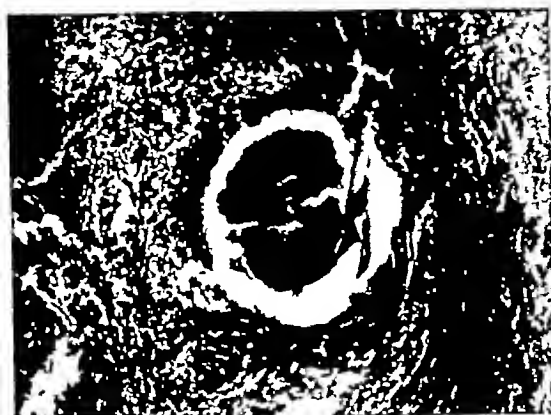


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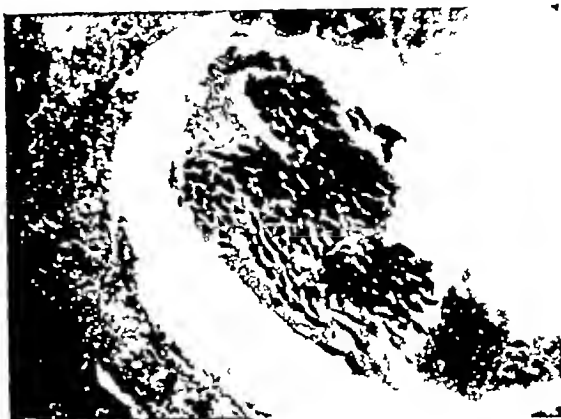


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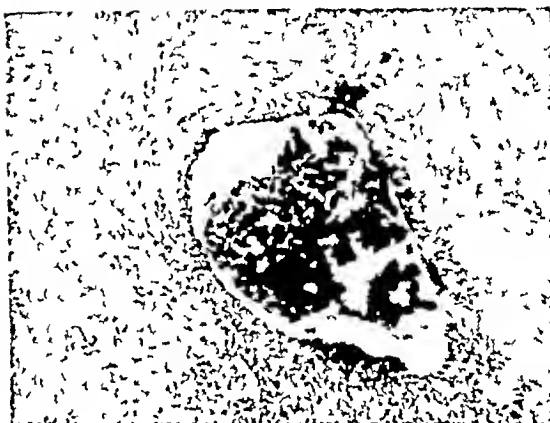


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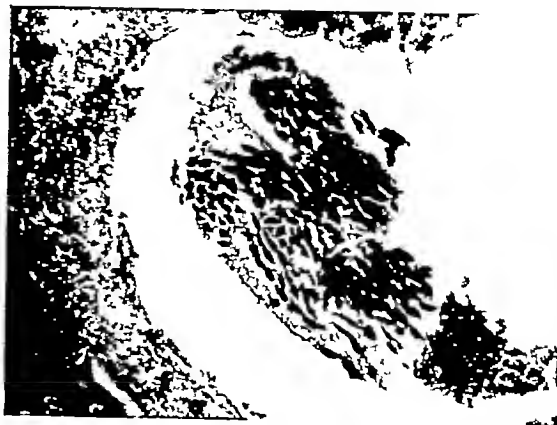


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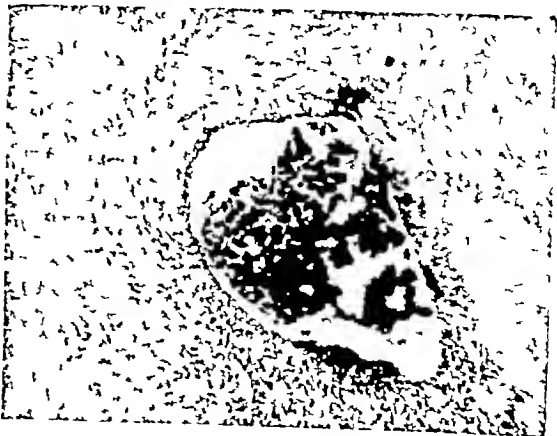


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CONCLUSIONS

1. Fine chromic catgut is more easily handled than silk of the same caliber.
2. The tissue reaction to fine silk in the mucosa resembles the reaction toward a

markedly foreign irritant. It is especially noticeable after 2 or 3 days when the unabsorbed silk produces pressure necrosis with sloughing of the mucous membrane.

3. Wound healing of the mucosa is more rapid when fine chromic catgut is used.

4. Fine absorbable catgut, designated No 00000 medium chromic, having an average diameter of 0.006 inch, has been shown to be superior to fine nonabsorbable black silk of equivalent size (No 0000 diameter 0.006 inch) as a suture material for the mucous membrane of the stomach because the silk produces pressure necrosis at the site of insertion with subsequent sloughing—as shown by redundant intraluminal loops.

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ARTERIOGRAPHY OF ABDOMINAL ORGANS BY AORTIC INJECTION

A Preliminary Report

O. A. NELSON, M.D., F.A.C.S., Seattle, Washington

IN this communication we shall deal with our experiences in making 73 renoabdominal arteriograms—roentgenologic delineations of the renal and abdominal arteries after aortic injection of a radio-opaque medium. By visualizing the arteries and thus tracing the blood supply, we demonstrate the location and size of the organs.

Information thus obtained is of great aid in the diagnosis of certain abdominal masses and tumors. Our arteriograms show that an abnormal contour or caliber of the arteries is concomitant with certain diseases of the arterial tree or organs. Sometimes the arteries of an organ containing a tumor or an inflammatory process are of larger caliber than normal. On the contrary, when there is sclerosis or fibrosis of an organ, the caliber of its arteries is diminished. Tortuosity of the arteries usually means arteriosclerosis.

Further, in cases of duplication of the renal pelvis—when one unit is so diseased as to necessitate heminephrectomy—arteriography is of value, as it is also in certain cases of aberrant blood vessels in relation to hydronephrosis. Arterial aneurysms are readily visualized by this procedure.

The most striking results appear in arteriograms of vascular neoplasms of kidney or suprarenal gland, in such cases pooling of the opaque medium in the blood sinuses is shown and is pathognomonic of these tumors. In papillary tumors of the renal pelvis and in other renal tumors without blood sinuses, such pooling or laking of course does not occur.

Much of the pioneer work concerning arteriography by aortic injection was done by Santos, Lamas, and Caldas (28). They have performed more than 2,000 aortic punctures for arteriography, and many more to mediate the blood stream for various types of in-

fection. These clinicians have also done outstanding work in roentgenography of the peripheral arteries.

The literature contains many articles on the subject, of which only a few were accessible to us. Castellanos and Pereiras describe a method of obtaining roentgenograms of the cardiac chambers and thoracic aorta by injecting and reversing the stream in the humeral or brachial artery. These workers used a 50 per cent solution of perabrodil or thoro-trast, and contended that their procedure was not harmful to the intima of the arteries so injected.

As early as 1923, Berberich and Hirsch did cerebral arteriography by injecting 25 per cent solution of sodium iodide into the common carotid artery.

Arteriography of the extremities has been done with a varying degree of success. Allen and Camp (1, 2) believe that it is technically quite feasible but rarely indicated, and that in the majority of conditions of the extremities diagnosis can be made without resorting to arteriography.

TECHNIQUE

For clarity, we shall first describe the technique used, and then discuss the untoward reactions.

There are 3 important basic requirements for production of these grams: (1) the skiagraphic medium must be concentrated, (2) the injection must be completed within a few seconds, (3) the exposure of the film must be made the instant that the injection is completed.

Equipment. As injection of the opaque medium and exposure of the film must be well co-ordinated, the time element in exposure is very important. Hand-syringe injection is

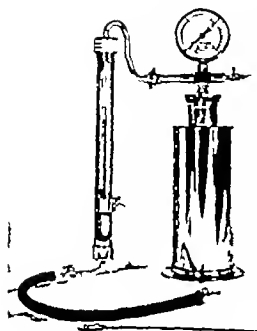


FIG. 1. Pressure apparatus.

unsatisfactory, so the equipment includes a pressure apparatus for injection of the solution (Fig. 1). One also needs an 18 gauge needle about 12 centimeters long and a supply of opaque medium. We use 80 per cent solution of sodium iodide. The x ray machine should have potential power to deliver 500 milliamperes of current and the Bucky diaphragm must be of the high speed type so that exposure can be made within one fourth of a second.

In the main we have followed the technique devised and practiced by Santos and his co-workers.

Preparation of the patient. On the afternoon before the examination the patient is given 2 ounces of castor oil preferably in fruit juice with a little soda or 3 ounces of castor oil in root beer. Thereafter he is allowed only liquid nourishment containing a minimum amount of fruit juice and sugar.

It is well to make a trial film before the aortic puncture when the patient is supine to show whether the patient is in proper position and the x ray technique satisfactory.

When this has been established the patient is anesthetized we prefer pentothal sodium.

The aortic puncture. After anesthesia has advanced so that reflexes are abolished the left side of the back and lower chest are prepared by tincture of iodine and draped with sterile towels.

The aorta normally lies along the left border of the vertebral column. Therefore, if a needle is passed from the back close to and a few centimeters beyond the body of a lower thoracic vertebra, it will enter the aorta. Figure 2 illustrates aortic puncture.

For arteriography of the kidneys and upper abdomen the needle is passed through the skin below the twelfth rib and three finger breadths to the left of the spinous processes. It is then directed toward the body of the twelfth thoracic vertebra. As soon as that bone is encountered the point of the needle is deviated slightly laterally so as to pass over the vertebra. When that is accomplished, the stylet is removed, and the needle gradually advanced a few more centimeters. Entrance into the aorta is signaled by blood coming through the needle. The needle is then advanced 1 more centimeter.

After one has advanced the needle and still observes free flow of blood, he can be certain that the needle is well within the aorta.

Injection of contrast medium and exposure of film. When the needle has been adjusted the pressure apparatus containing the opaque medium is attached to it. As soon as the x ray technician is ready to make the exposure the outlet valve on the pressure apparatus is opened, and 8 or 10 cubic centimeters of the contrast solution is allowed to flow into the aorta. If the pressure is set at one atmosphere or higher it takes only a few seconds to inject 8 or 10 cubic centimeters of 80 per cent sodium iodide. It is our practice to signal the x ray technician to make the exposure just before the valve on the pressure apparatus is closed. After the film has been exposed, the pressure apparatus is detached from the needle and a few cubic centimeters of blood is allowed to run out. Then the needle is withdrawn.

At The Swedish Hospital Dr. Blake has devised a lead shield over the Bucky diaphragm

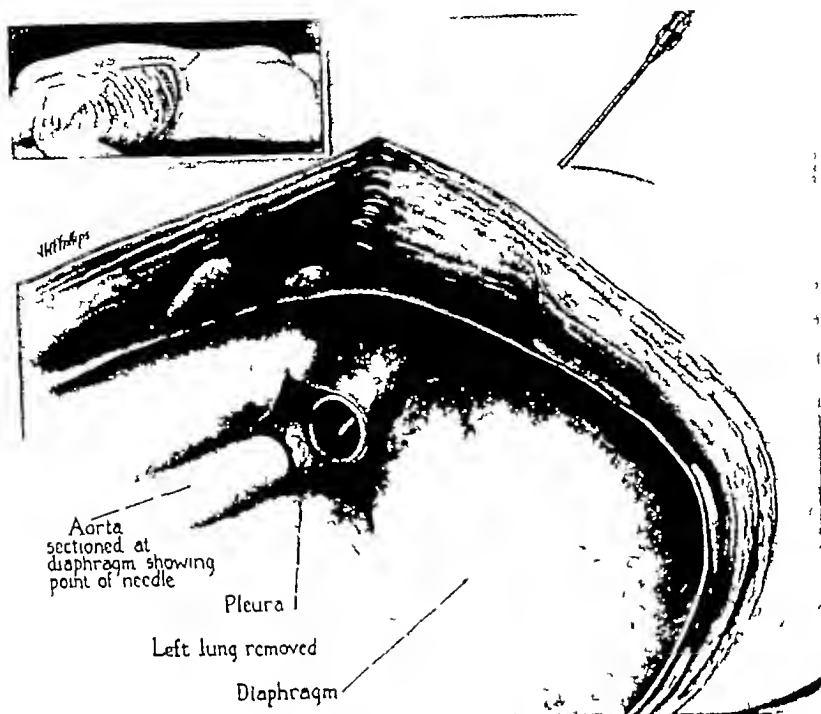


Fig 2 Aortic puncture

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Although tourniquets on the thighs to constrict arterial flow at the time of injection are advised by Santos, we have not used them.

UNTOWARD REACTIONS AND COMPLICATIONS

Iodism. On first learning of this procedure, one is likely to believe it is beset with frequent and severe untoward reaction. The only complication we have encountered is acute iodism.

As the flow of blood is very rapid through the aorta and its abdominal branches, the sodium iodide solution must be rather concentrated to give visualization of the smaller arteries, and about 8 or 10 cubic centimeters of it must be used. Consequently, the dose of sodium iodide is rather large. Acute iodism occurred in 4 patients in our series, but in none were the symptoms alarming. In fact, we have seen more severe iodism following excretory pvelography with an organic iodide solution, than after arteriography with sodium iodide.

Santos contends—and we believe it a fact—that a person can tolerate much larger doses of iodide, if it is injected into the aorta and goes through the capillary bed, than if injected into the vein or taken orally. We have seen patients who could not tolerate 1 gram of sodium or potassium iodide after meals three times a day, who had no disturbance from 10 grams of sodium iodide given into the aorta.

We have tried to ascertain whether sodium iodide in the aorta causes irritation of the intima of the arteries. We have studied histologically the arteries of kidneys removed immediately after the injection, and also the arteries of those removed some days after arteriography. In none were we able to find any evidence of change in the intima or arterial wall from the sodium iodide.

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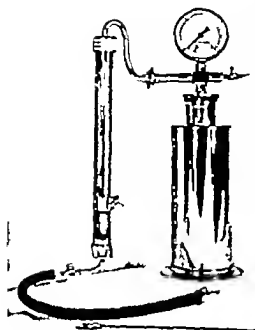


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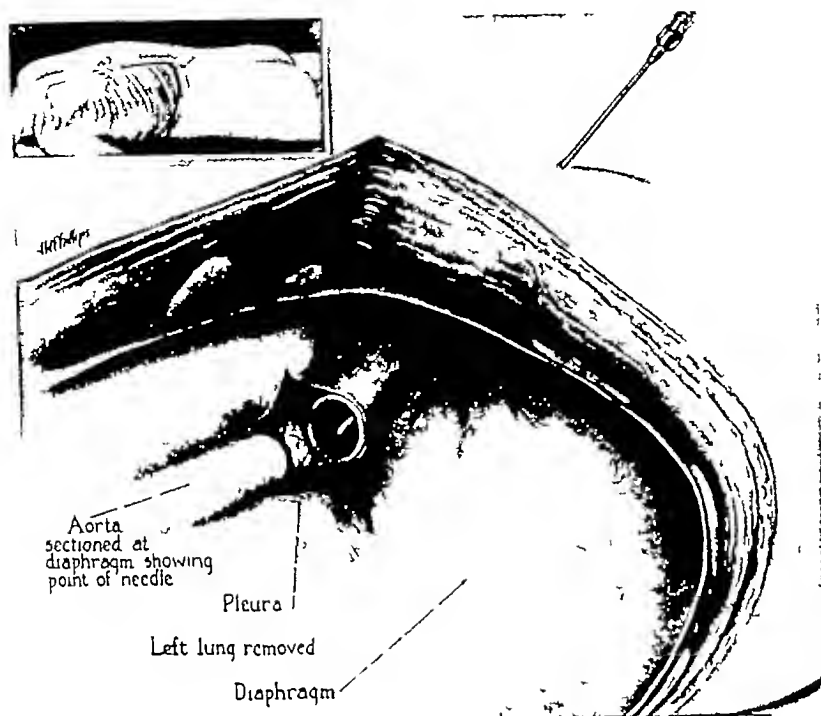


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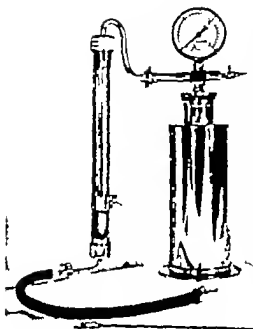


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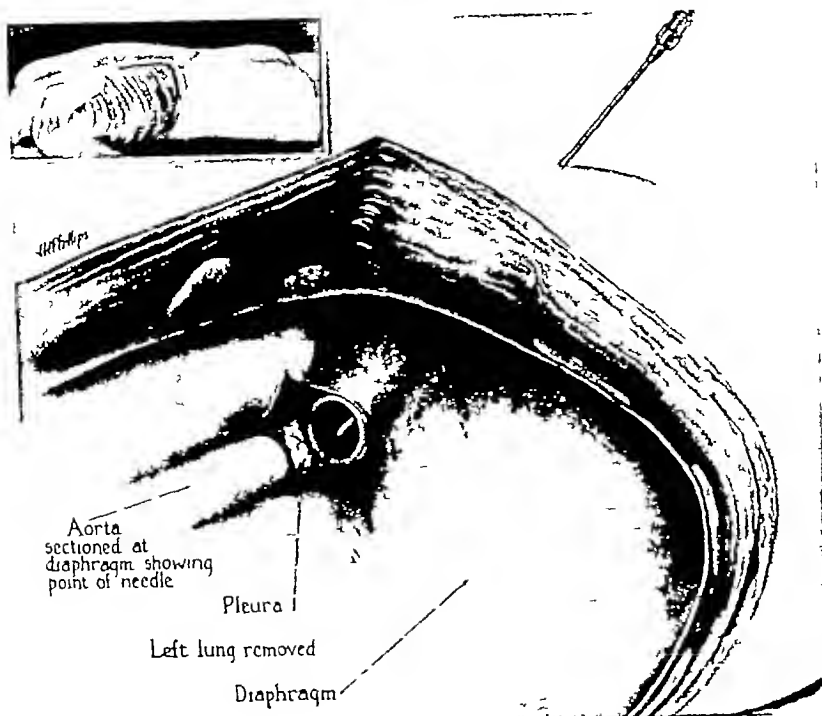


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Fig. 3. Arteriogram of normal arterial tree. a, aorta; b, splenic; c, gastroduodenal; d, renal; e, mesenteric arteries.



Fig. 4. Pooling of opaque medium outlines right renal tumor.

obtained marvellous excretory pyeloureterograms in patients whose renal function was too deficient to give satisfactory films after intravenous injection, and whose ureters could not be catheterized. Another type of interesting roentgenograms was developed in that some films show the outline of the renal parenchyma, making what we call renograms.

At present we have a biological chemist trying to ascertain the tolerance for sodium iodide injected into the aorta and the capillary bed, as compared with that when injected into the vein or taken by mouth.

We also have another chemist working on the problem of elimination of iodide through the kidneys after aortic injection, so that we may compare findings with iodide elimination after intravenous or oral administration.

While untoward reaction from the iodide has been neither severe nor frequent, it is to us the hazardous part of this procedure. We hope that in the near future a more satisfactory contrast medium will be found.

Injury to the aortic wall. Aortic puncture is not the formidable procedure it might seem. It should be remembered that the aorta has a thicker wall and will stand more trauma than any other blood vessel in the human body. It is a fact that in all the inadvertent aortic punctures made in attempting to produce splanchnic anesthesia complications are practically unknown. For a blowout or hematoma to occur from an aortic puncture the opening in the aortic wall must be large.

It goes without saying that anyone wishing to do an aortic puncture should familiarize himself very thoroughly with the anatomical parts involved, by doing several anatomical dissections. He should practice aortic puncture in the anatomical laboratory before puncturing the aorta in the living person. Santos advises against doing this on the dog, contending that it is not comparable to the human being as to arterial anatomy and physiology.

Extravasation of contrast solution. One complication that might seem dangerous is



Fig 5 Malignant tumor of right suprarenal gland. Note enlarged suprarenal artery, *a*, and pooling of medium *x*



Fig 6 Solitary cyst of left kidney. Note wide separation of spleen and kidney

extravasation of the opaque medium. But it has been found that 8 or 10 cubic centimeters of hypertonic sodium iodide solution is readily absorbed. Such an accident occurred twice in our early work. We now ascertain the position of the needle within the aorta before the injection is started. One of these accidents occurred in a patient suffering from melanotic sarcomatosis, who had a huge mass in the liver. He stated that there was no particular increase in the pain or backache after extravasation of 10 cubic centimeters of sodium iodide. The other patient was a woman in rather poor general condition. Because of her hirsutism and hypertension, an arteriogram was made to ascertain whether she had an adrenal tumor. After the periaortic injection, the right suprarenal gland was explored. At that operation the pleura was inadvertently opened. The patient suffered a massive collapse of the lung, and died on the third post-operative day. Postmortem examination

showed that massive collapse of the lung was the cause of death. There was a basophilic tumor of the pituitary gland. The tissue at the site at which the injection of iodide was made was red, but there was no evidence of necrosis.

It is not advisable to drain or explore, if periaortic injection occurs.

Our series of cases is yet too small to draw any definite conclusions. It is our impression that the procedure is valuable in certain diagnostic problems, and that it will yield information not obtainable by any other form of x-ray examination, nor even by surgical exploration, for even though a surgeon has a kidney in his hand, it is difficult at times for him to make a diagnosis with any degree of certainty.

The untoward reaction and suffering from arteriography of this type are usually less frequent and less severe than after retrograde pyelography.



Fig. 3. Arteriogram of normal arterial tree. Aorta, splenic, gastroduodenal, & renal, mesenteric, arteries.

Fig. 4. Pooling of opaque medium outlines right renal tumor.

obtained marvellous excretory pyeloureterograms in patients whose renal function was too deficient to give satisfactory films after intravenous injection and whose ureters could not be catheterized. Another type of interesting roentgenograms was developed, in that some films show the outline of the renal parenchyma, making what we call renograms.

At present we have a biological chemist trying to ascertain the tolerance for sodium iodide injected into the aorta and the capillary bed as compared with that when injected into the vein or taken by mouth.

We also have another chemist working on the problem of elimination of iodide through the kidneys after aortic injection, so that we may compare findings with iodide elimination after intravenous or oral administration.

While untoward reaction from the iodide has been neither severe nor frequent, it is to us the hazardous part of this procedure. We hope that in the near future a more satisfactory contrast medium will be found.

Injury to the aortic wall. Aortic puncture is not the formidable procedure it might seem. It should be remembered that the aorta has a thicker wall and will stand more trauma than any other blood vessel in the human body. It is a fact, that in all the inadvertent aortic punctures made in attempting to produce splanchnic anesthesia complications are practically unknown. For a blowout or hematoma to occur from an aortic puncture the opening in the aortic wall must be large.

It goes without saying that anyone wishing to do an aortic puncture should familiarize himself very thoroughly with the anatomical parts involved, by doing several anatomical dissections. He should practice aortic puncture in the anatomical laboratory before puncturing the aorta in the living person. Santos advises against doing this on the dog, contending that it is not comparable to the human being as to arterial anatomy and physiology.

Extravasation of contrast solution. One complication that might seem dangerous is



Fig 9 Large left hydronephrosis. The blood vessels can be traced going on outside of hydronephrotic sac. The outline of the parenchyma of right kidney can be seen.



Fig 10 A large calculus of right kidney. The arteriogram shows that there is a good blood supply to the kidney.

had had attacks of diarrhea and had noticed progressive weakness. For several months he had noted a mass in the left side of the abdomen. Pyelogram showed marked downward displacement of the left kidney with pyelectasis that was suggestive, but not diagnostic, of renal neoplasm. In the arteriogram the arteries in the spleen can be traced over the outline of the soft tissue shadow, showing that we were dealing with a case of splenomegaly. At the time the patient entered the hospital, the blood count was not definitely for polycythemia vera, but later showed the red count markedly elevated.

The following case is included to show the contrast between splenomegaly, pancreatic and renal cysts, and hydronephrosis.

Figure 9, case of Mrs. A. N. L., aged 31 years, who was referred for study because of pyuria and a mass and pain in the left side of the abdomen. During the last 3 years before our examination she had also had attacks of pain in the right kidney region. The urine contained many pus cells, with mixed pyogenic infection. Renal study showed, on the right side, a fair degree of renal function as measured by indigo-carmin. The pyelograms showed a moderately

large hydronephrosis, and an obstruction at the pelvoureter junction. On the left side, no urine could be obtained, and there was no evidence of dye secretion in 25 minutes. On this side all of the opaque medium injected for pyelography returned around the catheter into the bladder. The arteriogram showed the renal artery extending over a huge mass, without any of the blood supply going into the mass—which proved that we were dealing with an extensive hydronephrosis. After a plastic operation to correct the obstruction on the right side, a large hydronephrotic sac on the left side was removed. There was no evidence of parenchymal tissue.

Figure 10, case of Mrs. C. L., aged 60 years, who was referred for study and operation on account of pyuria and a shadow on the x-ray film of a large stone in the right kidney. The calculus filled the pelvis and calices of the kidney. The left kidney and ureter were normal. As the function of the kidney containing the stone could not be definitely ascertained, arteriography was advised and performed. The film showed ample blood supply to the kidney. However, at the operation nephrectomy was performed since it was found that the stone was very adherent to the mucosa of the kidney pelvis and calices.



Fig. 7. Pancreatic cyst. Although pyelogram is suggestive of renal tumor, arteriogram refutes that diagnosis.



Fig. 8. Splenomegaly. Note the course of arteries in the spleen.

CASE HISTORIES

In order to make our interpretations of the arteriograms clear we shall describe them. Figure 3 shows a practically normal arterial tree of the organs in the upper abdomen.

Figure 4, case of Mrs. L. C., aged 64. Patient gave a history of having had hematuria and pain in the abdomen, of 3 weeks' duration. Examination revealed a mass in the right kidney region, and gross hematuria, but no organisms were found in the urine. Study showed normal left kidney. The right ureter could not be catheterized. Consequently arteriography was recommended and done. The film showed a huge vascular tumor of the kidney. Findings at operation confirmed the diagnosis.

Figure 5, case of Miss N. Z., aged 39 years. Patient had marked bluntness of 1 year's duration. Although she had gained about 4 pounds in that time she had also had progressive weakness. Blood pressure was 80/30, and excretory pyelograms showed no abnormality of the urinary tract. An arteriogram showed a malignant tumor of the right adrenal gland. This tumor weighed 730 grams when removed at operation.

Figure 6, case of Mrs. A. G. M., aged 59 years, who underwent arteriography on August 5, 1937. A few days before that time retrograde pyelograms had been made which were suggestive of left renal neoplasm, with no history of hematuria or other clinical findings conforming to that diagnosis. Arteriogram showed upward displacement of the spleen and downward displacement of the kidney without blood vessels in the intervening tissue. From these findings diagnosis of renal or pancreatic cyst was made. Ten months later the operative finding was solitary cyst of the superior pole of the kidney.

Figure 7, case of Mrs. G. L. C., aged 4 years, who was referred on account of dull, aching pain in the left side of the abdomen, where a cystic mass about 6 centimeters in diameter could be palpated. There was a history of gross blood in the urine. Laboratory findings showed many red blood cells. Secretory pyelograms left us in doubt whether we were dealing with renal tumor.

The arteriogram showed the mass to be extra-renal. Diagnosis of pancreatic cyst was confirmed at operation.

Figure 8, case of M. J. H., Russian farmer, aged 64 years, who entered The Swedish Hospital April 1940. During the year previous to coming, he



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Fig 10 A large calculus of right kidney The arteriogram shows that there is a good blood supply to the kidney

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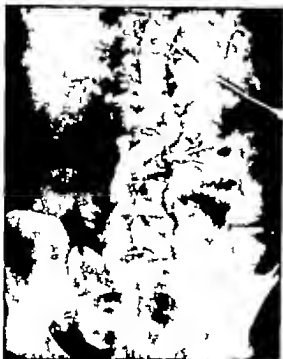


Fig. Atrophic pyelonephritis. Not the complete blockage of the left renal artery at the border of the splenic artery. The tortuosity of the aorta connotes advanced arteriosclerosis.

The patient has been examined about every 6 months since the operation, nearly 4 years ago. The urine and blood pressure have remained normal, and she feels well.

Figure 2 case of Mrs. F. L., aged 43 years, who gave history of having had nosebleeds on several occasions during the months previous to coming to the clinic on January 3, 1931. She was also extremely nervous. The salient points in the findings were pyuria and blood pressure of 140/60. Renal study showed practically normal kidney on the right side and atrophic pyelonephritis on the left. It seemed likely that we were dealing with case of Goldblatt kidney. The arteriogram showed obstruction in the renal artery short distance from the aorta, and attempt at establishing collateral circulation for it can be seen that small arteries bud out from the stem of the obstructed renal artery. The marked tortuosity of the aorta made it clear that she had advanced arteriosclerotic condition likely making hypertension irreversible. Four weeks after the arteriography left nephrectomy was performed. However there has been no material change in the blood pressure as it remained about 100/50. Her clinical condition symptomatically at least has improved.

SUMMARY

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SPONDYLITIS ADOLESCENS—STRUEMPPELL-MARIE DISEASE

Practical and Theoretical Considerations

HARRY C BLAIR, M D, Portland, Oregon

A PAPER by Scott, entitled "Spondylitis Adolescents with Associated Pathological Changes in the Sacroiliac Joints," was the inspiration for the present study. Scott suggested the name "spondylitis adolescents" for the ankylosing spinal arthritis which is found in young adults. And he was of the opinion that "wide field" radiation offered hope for patients suffering from this condition.

Spondylitis adolescents, designated variously as Struempell-Marie's disease, Bechterew's disease, ankylosing spondylitis, spondylose rhizomélisque, and spondylitis ankylopoetica, has for many years been differentiated from other types of arthritis. Yet this progressive and crippling disease, which ultimately leads to permanent deformity of the spine, had baffled all efforts to stop its course or to decrease the suffering and misery it causes until the introduction of roentgen therapy. When, however, the etiology and the pathology of this disease is considered, a number of questions arise. Why is spondylitis adolescents in the vast majority of instances to be found in young and otherwise healthy males? Why have pronounced changes already taken place in the sacroiliac joints, and often without the patient's having realized that anything is wrong, when symptoms of back pain first appear? Can a disease which is believed to be the result of an infectious process cause extensive destruction without giving rise to local pain or a general reaction? Why does this disease always involve both sacroiliac joints? Why are the sacroiliac joints, the spine, and occasionally the hip joints alone usually involved? Why are other joints ordinarily immune? Why if fusion has taken place in a hip joint and arthroplasty is attempted does immediate bony ankylosis occur? According to Buckley, Nelaton attempted arthroplasty three times on one patient, but even after

muscle had been imposed union took place. Is some metabolic process responsible for the destruction of connective tissue and cartilage? Iritis also occurs in this disease. Does a disturbance of the metabolic process control this?

In the present study, an attempt has been made to answer some of the questions raised. An attempt has also been made to determine the physiological action of roentgen rays inasmuch as in the cases reported herein, as well as elsewhere, roentgen therapy relieved pain and apparently also shortened the course of the spondylitis.

GENERAL CONSIDERATIONS

The clinical course of spondylitis adolescents is of long duration. The disease starts in early adolescence with indefinite low back pain and continues over many years with periods of remission and exacerbation. Pain may first be noticed at the age of 12, and ankylosis of the entire spine may not take place until the patient is 25 years of age or older. With ankylosis the active part of the disease is thought to be at an end. The previous clinical history at the time of the first examination may be short—a month or 6 months. Yet roentgenograms usually show advanced changes in the sacroiliac joints, indicating that these changes do not necessarily cause pain, disability, or other symptoms.

The erythrocyte sedimentation rate is usually increased in spondylitis adolescents, sometimes to a considerable degree. Apparently this increase is proportionate to the extent of involvement and the amount of activity visible in the roentgenograms. The sedimentation rate is said to indicate the infectious etiology of spondylitis. Inasmuch as the exact relationship of the sedimentation phenomenon and infection is not known, and inasmuch as the sedimentation rate is also in-



Fig. Atrophic pyelonephritis. Note the complete blockage of the left renal artery at the border of the splenic artery. The tortuosity of the aorta associates an aortic arteriosclerosis.

The patient has been examined about every 6 months since the operation, nearly 4 years ago. The urine and blood pressure have remained normal, and he feels well.

Figure case 3 Mrs F L, aged 4 years, gave history of having had nosebleeds several occasions during the months previous to coming to the clinic July 3, 1934. She was also extremely nervous. The salient points of the findings were pyuria and blood pressure of 140/60. Renal study showed practically normal kidney; the right side atrophic pyelonephritis on the left. It seemed likely that we were dealing with case of Goldblatt kidney. The arteriogram showed obstruction in the renal artery short distance from the origin and attempt to establish collateral circulation for the case to be seen that small arteries had cut from the stem of the obstructed renal artery. The marked tortuosity of the aorta made it clear that she had advanced arteriosclerosis, condition likely making hypertension irreversible. Four weeks after the arteriography left nephrectomy was performed. However there has been no material change in the blood pressure as it remains about 100/50. Her clinical condition symptomatically at least has improved.

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muscle had been imposed union took place. Is some metabolic process responsible for the destruction of connective tissue and cartilage? Iritis also occurs in this disease. Does a disturbance of the metabolic process control this?

In the present study, an attempt has been made to answer some of the questions raised. An attempt has also been made to determine the physiological action of roentgen rays inasmuch as in the cases reported herein, as well as elsewhere, roentgen therapy relieved pain and apparently also shortened the course of the spondylitis.

GENERAL CONSIDERATIONS

The clinical course of spondylitis adolescents is of long duration. The disease starts in early adolescence with indefinite low back pain and continues over many years with periods of remission and exacerbation. Pain may first be noticed at the age of 12, and ankylosis of the entire spine may not take place until the patient is 25 years of age or older. With ankylosis the active part of the disease is thought to be at an end. The previous clinical history at the time of the first examination may be short—a month or 6 months. Yet roentgenograms usually show advanced changes in the sacroiliac joints, indicating that these changes do not necessarily cause pain, disability, or other symptoms.

The erythrocyte sedimentation rate is usually increased in spondylitis adolescents, sometimes to a considerable degree. Apparently this increase is proportionate to the extent of involvement and the amount of activity visible in the roentgenograms. The sedimentation rate is said to indicate the infectious etiology of spondylitis. Inasmuch as the exact relationship of the sedimentation phenomenon and infection is not known, and inasmuch as the sedimentation rate is also in-

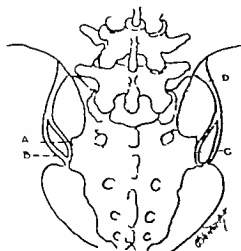


Fig. Outline of the normal sacroiliac joints of an adult. A, posterior view; B, anterior view; C, cartilaginous section; D, fibrous section (Scott).

creased in other destructive conditions, such an assumption is tenable only as presumptive evidence. The patients under my observation had all been healthy young individuals prior to the onset of back pain, and some had been subjected to rigorous examinations for foci of infection. The search for infection had been followed by all the usual types of treatment—removal of tonsils and suspicious teeth, sinus operations, stool cultures, vaccine and all forms of physiotherapy and supports. In no instance, however, had the course of the spondylitis been shortened. In spite of the varied treatment more and more joints had become involved. Flexion of the spine had increased and the disease had progressed until complete ankylosis had taken place.

If a general metabolic change is responsible for the absorption of cartilage, it is reasonable to suppose that absorption would begin in an area of low vitality. Disease or destruction of a joint produces immobilization in that joint. Although immobilization is nature's method of relieving pain, it accelerates the absorption of cartilage and the atrophy of bone. And the process spreads until ultimately all cartilage is absorbed and bony ankylosis supervenes. The sacroiliac joints contain large amounts of cartilage. Normally there is very little movement in these joints. The tissues here there-

fore are of low relative vitality. In spondylitis adolescents the sacroiliac joints are the first to be attacked by the fixation process. Fixation next takes place at the lower spinal segments because the muscles that control their movements to some extent also control the movements of the sacroiliac joints. Eventually the process extends to all the joints of the spine with the exception of the upper two cervical segments. And the cervical segments are spared because movements of the head or neck are normally relatively excessive. This progressive fixation is carried out in the same sequence in the hip joints. Movements of rotation and abduction are the first to be lost and are the least disabling because they are used least often in ordinary activity. Movements of flexion and extension are the last to be lost because they are used most often.

Roentgenographic examination is depended upon for an insight into the pathology of spondylitis adolescents since there are no early autopsies. The first abnormal change noted in the roentgenograms is a widening and an irregular fuzziness of the sacroiliac joints. Areas of localized bone absorption occur nearby or general atrophy of the adjacent sacrum or ilium ensues. This, however, is usually 'spotty' in character. The cartilage is absorbed, the joints as such disappear and bony ankylosis takes place. This is usually followed by increased density of the bones in the sacroiliac region. The same process takes place in the remainder of the spine. The posterolateral articulations disappear as their cartilage is absorbed. The bodies of the vertebrae show considerable halisteresis. And as remission takes place it is seen that the supporting ligaments have been involved since they become calcified and later ossified. This calcification and ossification do not appear to spread to other soft tissues in the body. The intervertebral discs do not lose width but show more or less calcification. Bechterew described a similar disease which involved the dorsal vertebrae first. One of the patients in the present group is thus classified. It is significant that both sacroiliac joints were involved when this patient first complained of thoracic pain. Scott called attention to the fact that there is as yet no satisfactory explanation for



Fig. 2, 1 and 2. Advanced case of spondylitis adolescens with complete ankylosis of the hip joints, sacroiliac joints and spine. It will be noted that the cartilage in the sacroiliac joints has been completely absorbed and is replaced by what is apparently normal bone. In the lateral view of the spine, 1, it is seen that the width of the intervertebral discs has not changed.

the absence of sacroiliac pain during the active period of the disease

ROENTGEN THERAPY

In Scott's opinion, roentgen therapy brings about some beneficial constitutional effect which suggests stimulation, or the reverse, of the ductless gland system. He advised that roentgen therapy for spondylitis adolescens be instituted early. But he warned against the use of high voltage roentgen therapy, and stated that serious damage could be done if large doses were used.

Smyth, Freyberg, and Peck called attention to the fact that subjective benefit following roentgen therapy may be of psychogenic origin. They reported 15 cases of spondylitis rhizomélisque in which roentgen therapy had been used. In 74 per cent of these cases there was definite subjective and objective evidence of benefit, and in 67 per cent the beneficial results were permanent. After careful search for a reason why roentgen therapy is bene-

ficial, they did not even find a theoretical explanation for its use. And they concluded that "the rationale for employment of roentgen therapy in rheumatic disease and its *modus operandi*" was a complete mystery to them.

In the present series of cases the "wide field" technique described by Scott was followed. The roentgen rays were of medium wave length, were passed through thin filters, and were distributed over a large body area. Treatments were given twice a week for 16 doses, the total dosage being 1000 roentgens. When it was deemed necessary, the treatment was repeated. There were no serious reactions of any kind. Some of the patients complained of slight nausea, but the treatments caused no real inconvenience. No other therapy was used. Vaccine, physiotherapy, braces when possible, and all analgesics were abandoned so that a better estimate of the results might be made.

It is generally realized that remissions do take place in spondylitis adolescens and that

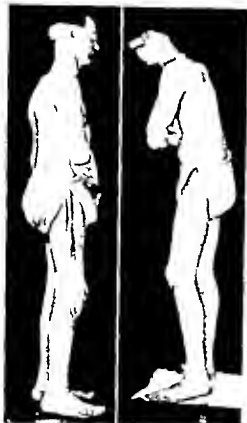


Fig. 3. and b T. brothers ichthyospondylitis. Although both of these patients are subjected to rigorous exercise tests, no infectious foci were found.

spontaneous recovery may take place also that the course of this disease is from 10 to 20 years, and that sufficient time has perhaps not yet elapsed to evaluate properly the results from roentgen therapy. On the other hand reports in the literature show an increasing number of encouraging results following the use of irradiation for this condition. Even though the present series is small and it has been only 4 years since the first treatment was given improvement has been so consistent in the comparatively early cases that it is felt the results obtained are worthy of being reported.

CASE REPORTS

CASE. W. H. male aged 4 years, was first seen on January 3, 1938, complaining of pain. His back had appeared first in the left hip then in the right



Fig. 4. Following arthroplasty there is defect tendency for any loss to take place. The roentgenogram illustrates this phenomenon.

stiffness of the back and pain under the costal margin. Symptoms were of 3½ years duration.

The first irradiation treatment was given on December 9, 1935. The patient felt worse after this therapy, however, was continued, and the series of 6 treatments was completed January 3, 1939. Three days later the pain was no better than it had been. The result of the roentgen therapy, improvement, however, was noticed within a few weeks, and continued over the succeeding 3 years. The patient, as employed, tentatively played tennis and golf and continued swimming. He had only an occasional large

Roentgenogram plus find 17. The first roentgenogram which the patient brought with him, had been taken on December 30, 1935. It as interpreted in the erect view did show an irregular outline of the sacroiliac joints and roughening of the lower lumbar posterolateral joints. Roentgenogram on January 4, 1938 showed considerable increase of the irregularity of these joints. The joint spaces were widened, and the adjacent bone as mottled in some areas the bone as dense in others trophic. The bodies of the last lumbar vertebra had fuzzy appearance. The posterolateral joints were not visible. On January 24, 1939, 4 years after irradiation, roentgenogram showed the sacroiliac joints to be completely fused. Bone striations had approached normal, and the increased density had disappeared. The texture of the vertebral bodies had lost its fuzzy appearance. And the two lower vertebral joints appeared to be ankylosed.

This boy's condition had grown progressively worse until he was treated with roentgen rays. Since then his symptoms continued to decrease. Roentgenograms revealed that the

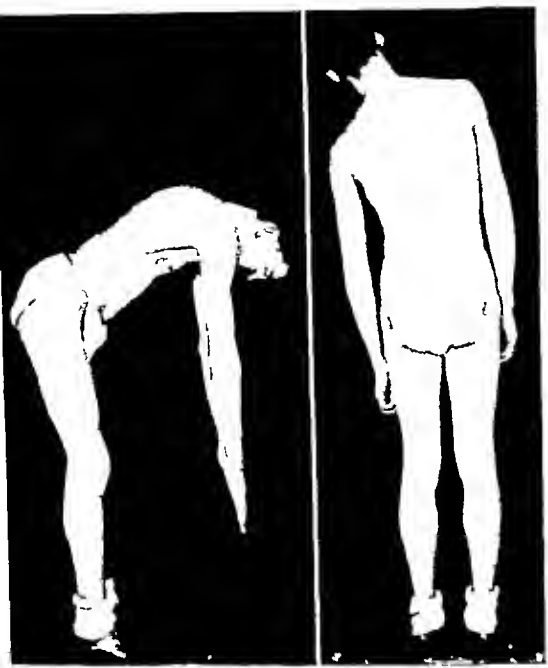


Fig 5, a and b These photographs were taken some months after a course of roentgen therapy. There were no complaints of pain at that time, but rather pronounced rigidity was still present. At the beginning of the treatment this boy was walking on crutches because of pain.

texture of the bone in the involved areas had improved considerably. Ankylosis of the involved joints had, however, continued. It may be argued that this is a natural recession, as sometimes occurs in this disease. It was not caused by the psychologic effect of treatment since improvement did not take place until after the treatment was stopped.

CASE 2 A G, male, aged 18 years, was first seen on December 16, 1935 because of painful feet. At that time the patient had no symptoms referable to the back. On September 15, 1938, however, he complained of severe back pain with stiffness of the back and hips and flexion of the hips and spine.

A series of 16 roentgen treatments was started on March 14, 1939. This was followed by striking symptomatic relief, but the stiffness of the back and hips remained the same. On October 23, 1939, he returned. He was walking with the aid of crutches, and complained of severe pain in the lower back. Another series of roentgen treatments was started. Improvement during this treatment course was remarkable. Within a week the crutches were discarded. On January 18, 1940, the patient reported that he had no pain. He had gained 20 pounds. There was increase in the movements of the hips



Fig 6 While there are definite abnormal changes in the sacroiliac joints shown here, the changes consist only of irregularity of the anterior fissure and sclerosis of the adjacent bone, the ilia, and the sacrum. This indicates that spondylitis may not progress to complete ankylosis.

and probably also of the spine although this is difficult to estimate.

CASE 3 B C, male, aged 15 years, was first seen on June 5, 1940 complaining of back pain of 1 year's duration. No other joints were involved. The tonsils had been removed.

Examination revealed loss of normal lumbar lordosis. There was a slight flexion deformity of the hips (psoas spasm). The hip movements were normal otherwise, except for slight restriction of external rotation. Roentgenograms were normal except for slight irregularity of the sacroiliac joints and some widening. The bone texture was good. There was no evidence of involvement of the posterolateral vertebral joints from the roentgenographic standpoint, but clinical findings were very definite.

After 4 roentgen treatments the patient was not so stiff as he had been. Improvement continued without interruption. This patient, who had been so disabled that he could not take part in games or sports, was playing football by October, 1940. He had no pain, and almost all of his back stiffness had disappeared by that time. Roentgenograms taken on June 2, 1941, showed normal sacroiliac joints. There was no clinical evidence of disability, and there were no complaints. This boy gained 15 or 20 pounds, and was in excellent health.

CASE 4 D MacD, male, was first seen when he was 32 years old. When he was 16, he had noticed pain and swelling in his feet. Later he had also had pain in his back. No other joints had been involved.

Roentgenograms revealed extensive involvement of the bones of the pelvis and of the entire spine. Atrophy was pronounced. There was also fusion of the sacroiliac joints, some deformity of the pelvis, and ankylosis of the spine.

On December 8, 1938, roentgen therapy was started. After the first 8 treatments roentgenograms



Fig. 7. Myofascial contractures of long standing. This patient suffered for many years with spondylitis adolescents. About the time of the onset of his spinal symptoms he also developed the condition in his thigh which is shown in this roentgenogram. Some disturbance of the heparin content of the blood or the tissues may be responsible for this process.

showed beginning collapse of some of the vertebral bodies. This collapse had taken place while the patient was wearing a T 12-16 back brace and during the time he was being given radiotherapy. Treatments were stopped. The patient, however, began to improve. He gained 20 pounds and the swelling of his feet subsided. On November 8, 1930, treatments were resumed and 6 were given. Roentgenograms of the lumbar spine on April 24 showed that recalcification was taking place. The patient in general condition at that time was greatly improved. His appetite was better, the pain was less severe, and he was able to return to his work as salesman.

Improvement in this instance took place at a time when retrogression of symptoms might be expected. Nevertheless, the improvement seems to have been directly associated with the roentgen therapy, since no improvement had occurred with any other form of treat-

ment. It is of interest to note that this patient's brother also had spondylitis adolescents. The brother, however, had no irradiation, and the disease progressed to ankylosis in spite of every known type of therapy.

CASE 5. A. R. male, aged 33 years, as first seen on April 20, 1930. I. 936 this patient had injured his back. He had taken no chiropractic treatments, but in spite of this he had become almost completely disabled. On December 9, 1938, 4 1/2 months before admission, he had got injured his back while lifting a sack of wheat and throwing it into a truck. Following this he had pain across his hips.

Examination revealed stiffness of the spine and muscle spasm. There was some interference with straight leg raising. Roentgenograms showed irregularity of the sacroiliac joints with sclerosis of the adjacent bone and some decreased definite markings of the lower lumbar posterolateral articulations.

Irradiation was started on April 20, 1930. On June 3 the patient returned to work. On December 1930, he reported that he had twisted his back and that this had caused a return of the pain. He stated, however, that the roentgen therapy had done him a great deal of good, that it had taken much of the stiffness out of his back and that he did not have the catches in his hips and back that he had had before.

Both sacroiliac joints of this patient were abnormal. The changes, however, consisted only of an irregularity of the joint outlines. It is possible that in some instances spondylitis adolescents does not progress to ankylosis.

RELATIONSHIP OF MAST CELLS AND HEPARIN TO SPONDYLITIS ADOLESCENS

It has been demonstrated that the mast cells of Ehrlich are present in wide distribution in the body and are especially abundant in the connective tissue surrounding blood vessels. It has also been shown that the distribution of these cells is proportionate to the abundance of heparin in the various organs. Holmgren and Wilander found that heparin is contained in the granules of the mast cells. Before this, Lison had observed that the presence of mucosin and chondroitin sulfuric acids is responsible for the metachromatic reaction shown by mucoid and cartilaginous tissues when stained with toluidine blue and that this staining reaction is specific for these sulfur acid esters of high molecular weight. And Jorpes pointed out that heparin, which is a polysulfuric ester with a high molecular

weight, gives a color "a hundred times stronger than that obtained with the same quantity of chondroitin sulphuric acid," also, that "toluidine blue possesses an extremely strong affinity for heparin"

In an excellent and exhaustive review of the chemistry, physiology, and clinical application of heparin, Mason called attention to the fact that "the ester sulfate content of tissues was found to parallel its content in mast cells, as was the content of crude heparin. The morphologic and chemical observations," he stated, "all strongly support the conclusion that (1) the metachromatic granules in these cells contain heparin, (2) that the cells have secretory activity, and (3) that their function is to supply the circulation with the physiologic anticoagulant." Mason cited the important studies carried out by Jorpes and his associates on the chemistry of heparin, and he summarized Jorpes' chief contentions as follows: Heparin is a mucoitin polysulfuric ester of variable composition—these variables being the number of sulfuric acid groups substituted into the individual mucoitin units, the degree of polymerization (the number of mucoitin sulfuric acid units which are linked together to form its polysaccharide structure), and the relative esterification of each unit. Chondroitin and mucoitin sulfuric acids, Mason explained, "are the prosthetic groups of the corresponding chondroproteins and muco-proteins. They consist of units of an hexuronic acid, presumably glycuronic, an amino sugar, sulfuric and acetic acids. The acetic acid is present as an N-acetyl group on the amino sugar, and sulfuric acid, one or more moles, is bound by an ester linkage to the free hydroxyl groups of the hexuronic acid and/or the hexosamine, the latter being galactosamine in chondroitinsulfuric acid and glucosamine in mucoitinsulfuric acid."

Cartilage is composed of approximately 70 per cent water, 28 per cent organic solids, and 2 per cent inorganic matter. The organic solids are for the most part chondroitin sulfuric acid. Chondroitin sulfuric acid is found not only in cartilage but also in tendons, ligaments, aorta, sclera, and probably, according to Levene, in osseomucoid. Logan stated that the conversion of cartilage to organic matrix

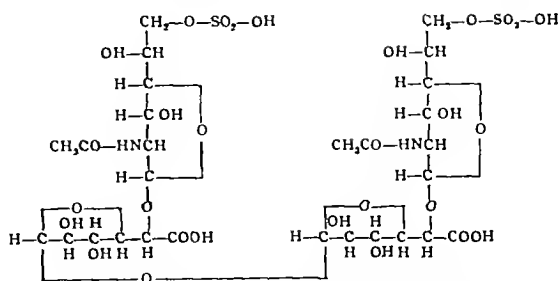


Fig 8 Structural formula of chondroitin sulfuric acid (Levene) Chondroitin sulfuric acid contains galactosamine. Mucoitin sulfuric acid (heparin) contains glucosamine. The hydroxyl on the fourth carbon of the hexosamine group is inverted in mucoitin sulfuric acid as compared with chondroitin sulfuric acid. These compounds are closely allied in their physical and chemical properties.

of bone is characterized by the loss of organic sulfates.

Tumors such as carcinoma are surrounded by a great number of mast cells. After treatment with high voltage roentgen therapy the mast cells disappear. Sylvén attempted to determine what happened to mast cells after such therapy, and conducted experiments on rats. The animals were covered with lead plates except for a field on the abdominal wall measuring 5 by 5 centimeters. Two series of animals were given 1000 and 1500 roentgens, respectively, in one treatment. One or two days after irradiation there appeared in all connective tissue of the corium and the subcutis substances exhibiting metachromatic staining reaction. These substances were diffusely distributed in the cell territories of the fibroblasts. Sylvén observed that after treatment of low dosage, 1000 and 1500 roentgens, a great many granules in the mast cells had disappeared, but there had been no increase or decrease in the number of mast cells. The results indicate that some of the sulfuric acids in the granules was excreted from the cytoplasm of the mast cells and spread diffusely over the surrounding connective tissue after exposure to roentgen rays. The threshold dose seems to be less than 1000 roentgens. Smyth *et al* used 600 roentgens in 3 doses in treating spondylitis.

IRITIS

It has been noted by many observers that iritis occasionally occurs during the course of

spondylitis adolescens. In the cornea there are normally very few mast cells but during the course of an infection such as a serpyginous ulcer the number of these cells increases. There is also an increase of the mast cells in the eye when iritis and glaucoma occur. The aqueous and vitreous humors consist of mucicillin sulfuric acid. The fact therefore that the eye is composed of substances closely related to the chondroitin sulfuric acid of cartilage together with the fact that the eye is involved during the course of spondylitis adolescens, indicates a direct relationship of metabolic origin. Furthermore the increase of the mast cells may be an effort toward healing. Ehrlich in 1879 stated that these cells were related to the nutrition of tissues. Because of this he labelled them mast (food) cells.

EVALUATION

It would seem logical to believe (1) that the pathological changes which occur in spondylitis adolescens are caused by an absorption of cartilage and not by an infectious process (2) that the beneficial results obtained from the generalized exposure of the body to roentgen ray dosage of medium wave length is brought about by the liberation of sulfur within the body in such a form that it can replenish a sulfur deficiency in any part of the body (3) that in spondylitis adolescens chondroitin sulfuric acid is absorbed from the cartilage, ligaments and bone in and around the sacroiliac joints and spine and (4) that this absorption probably occurs because of a deficiency of sulfur or mucicillin or chondroitin sulfuric acids elsewhere in the body. It is of interest to note that Cawadiaz in 1923 stated that it is not illogical to assume that a certain hereditary or constitutional predisposition exists for sulfur demineralization. He expressed the belief that sulfur demineralization is a special metabolic disturbance in rheumatoid arthritis, and that the tissues in this condition lose the power which they have of retaining sulfur.

SUMMARY

1. Cartilage consists of chondroitin sulfuric acid a substance like mucicillin sulfuric acid.
2. Mast cells contain granules composed of mucicillin sulfuric acid. These cells are located mostly in the connective tissue around blood vessels as well as in synovial tissue.
3. Irradiation causes mast cells to give up their sulfuric ester granules.
4. Roentgen ray dosage of comparable strength gives striking relief of the symptoms associated with spondylitis adolescens.
5. The hypotheses are presented (1) that spondylitis adolescens is caused primarily by an absorption of cartilage from the joint involved and not by an infectious process (2) that the beneficial results of roentgen therapy are brought about apparently by liberation of sulfur within the body in a usable form and (3) that iritis a condition associated with spondylitis, is caused by the same metabolic disturbance and possibly may react favorably to the same treatment.

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A CLINICAL AND PATHOLOGICAL STUDY OF LEIOMYOSARCOMA, HEMANGIOENDOTHELIOMA OR ANGIOSARCOMA, AND FIBROSARCOMA OF THE STOMACH

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A GREAT deal has been written on the subject of sarcoma of the stomach, although it is a comparatively uncommon lesion. Much confusion has resulted from the lack of a uniform nomenclature and classification for these tumors. It is our belief that the leiomyosarcomas, hemangioendotheliomas and fibrosarcomas of the stomach comprise a group of nonepithelial neoplasms quite distinct clinically and pathologically from the group of lymphosarcomas. The purpose of this paper is to correlate the clinical and pathological features of sarcoma of the stomach with special reference to the foregoing three types and to present a simplified classification.

Fourteen histologically proved cases of gastric sarcoma, exclusive of lymphosarcoma, in which operation was performed at the Mayo Clinic between 1908 and 1938 inclusive, have formed the basis for this paper.

The first case of sarcoma of the stomach in the literature was that recorded by Bruch in 1847. In 1901 Fenwick reported 53 proved cases of sarcoma of the stomach and in 1914 Forni made a complete analysis of the subject, bringing the total cases reported to 200. A review of the literature in 1930 by D'Aunoy and Zoeller increased this figure to 335 cases.

ETIOLOGY

As in all forms of malignant lesion, very little is known concerning the causation of gastric sarcoma. Various hypotheses have been advanced but in general it may be said that probably no single specific factor is responsible for the origin of sarcoma. Trauma,

inflammation, or some form of chronic irritation is believed to act on normal tissue cells, benign tumors, ulcers, or congenital isolated cell rests of the stomach to produce proliferation of mesoblastic cells and ultimately sarcomatous change.

Trauma is thought to play an important etiological rôle. Numerous cases are cited in which the patient associated the onset of symptoms with some form of trauma, and such observers as Brooks, Sherrill and Graves, and McWhorter have called attention to this relationship.

Farr explained the relative infrequency of sarcoma of the stomach as compared with carcinoma by the fact that the connective tissue elements of the stomach from which sarcoma takes its origin are less exposed to injury than the carcinoma forming epithelial surfaces which are exposed constantly to chemical and mechanical assault.

Some observers contend that sarcomas do not develop from previously normal cells but rather from congenital cell rests, but this contention has not been proved. Mallory stated that hemangioendotheliomas are often congenital and frequently, perhaps always, arise from abnormalities of the blood vessels.

There is little doubt that sarcomatous change does occur occasionally in benign gastric tumors and may even take place rarely in chronic gastric ulcers. This relationship has not been proved satisfactorily but has been suggested many times. D'Aunoy and Zoeller claimed that it is theoretically possible because gastric ulcers can stimulate prolonged formation of connective tissue, and such chronic reactions to irritation have been shown conclusively to act as etiological factors in the production of malignant processes in other organs.

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Abridgement of thesis submitted by Dr. Lemon to the Faculty of the Graduate School of the University of Minnesota in partial fulfillment of the requirements for the degree of M.S. in Surgery.

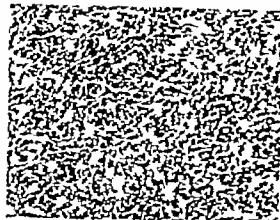


Fig. 3

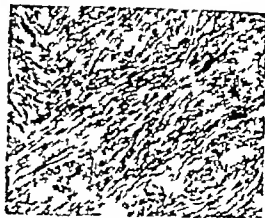


Fig.

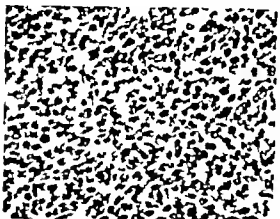


Fig. 3



Fig. 4



Fig. 5

Fig. 3. Leiomyosarcoma of the stomach of low grade malignancy (hematoxylin and eosin, $\times 30$).

Fig. 4. Benign leiomyosarcoma of the stomach showing mature smooth muscle tissue in its characteristic arrangement. No mitotic figures are present (hematoxylin and eosin, $\times 30$).

Fig. 5. Highly malignant leiomyosarcoma of the stomach. Note the solid growing, highly undifferentiated cells and the presence of mitotic figures (hematoxylin and eosin, $\times 34$).

Fig. 6. Hemangioendothelioma, or angiosarcoma, of the stomach. Notice how the endothelial cells, in an attempt to form new vessels, have arranged themselves into cord like structures some of which have already been cannalized and contain erythrocytes (hematoxylin and eosin, $\times 30$).

Fig. 7. Fibrosarcoma of the stomach. Fibrocytoma changes (hematoxylin and eosin, $\times 30$).

In this series 8 of 14 patients, or 57.1 per cent, had one or more reasonably definite features of ulcer. These consisted of periodicity, epigastric pain coming on after meals, relief of pain after ingestion of food and alkali, nocturnal pain, and a history of previous roentgenological diagnosis of ulcer. The preoperative clinical diagnosis in 2 cases was peptic ulcer, while in 3 cases a roentgenological diagnosis of ulcer had been made previously.

Incidence Sarcoma has been estimated variously to comprise from 1 to 8 per cent of all neoplasms of the stomach. Ewing estimated its frequency at 1 per cent, while Fenwick expressed the opinion that it comprises from 5 to 8 per cent of all gastric neoplasms.

Age Sarcoma of the stomach affects all age groups, although the period between 40 and 60 years of age comprises the largest group. The youngest patient appearing in the literature is that reported by Finlayson, a child 3 years of age with a fatal outcome 6 months later. The oldest patient, 91 years of age, was reported by Di Giacomo.

The average age of patients who have gastric sarcoma is considerably less than that estimated for carcinoma. Douglas quoted the average age for gastric carcinoma from the United States census figures as 61.2 years.

In this series the average age of the patients was 43.2 years, the youngest being 10 years of age. Almost half of our patients fell in the age group of 40 to 50 years. In 11 of our 14 cases the lesion was leiomyosarcoma, the average age of the patients was 46.6 years. There were 2 cases of hemangioendothelioma, in which the patients were 10 years and 29 years of age, respectively. In the case of fibrosarcoma the patient was 54 years old.

Sex The average reports in the literature state that the sex is divided about equally, although such observers as Balfour and McCann, and D'Aunoy and Zoeller report a preponderance in males.

In our 14 cases, 9 of the patients, or 64.3 per cent, were males and 5, or 35.7 per cent, were females. Only 3 of the 11 leiomyosarcomas were found in females while both of our cases of hemangioendothelioma were in females. The 1 case of fibrosarcoma occurred in a male.

PATHOLOGY

Attempts to classify sarcomas of the stomach pathologically have met with varying degrees of success. Seventeen different classifications have been encountered in the literature and these appear to have little uniformity.

It is apparent, therefore, that some simple inclusive classification should be decided on. It is recognized fairly generally that lymphosarcomas make up a definite class of gastric tumors, not only clinically and pathologically, but also in regard to their treatment and prognosis. The remaining types of gastric sarcoma, which comprise about a fourth of the total number, may be divided into three groups: leiomyosarcoma, hemangioendothelioma or angiosarcoma, and fibrosarcoma.

Frequency Confusion exists regarding the relative frequency of the different histological types of gastric sarcoma. Fenwick stated that lymphosarcoma comprises 62 per cent of the sarcomas of the stomach, fibrosarcoma, 22 per cent of the cases, and leiomyosarcoma and angiosarcoma make up the remainder.

In Balfour and McCann's 54 cases, lymphosarcoma comprised 71.3 per cent, fibrosarcoma 13.3 per cent, and myosarcoma 6.7 per cent.

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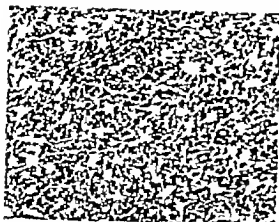


Fig. 2

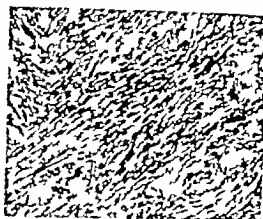


Fig. 3

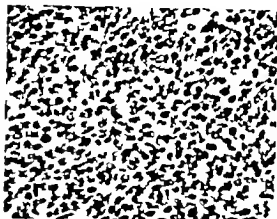


Fig. 4



Fig. 5



Fig. 6

Fig. 1. Leiomyosarcoma of the stomach of low grade malignancy (hematoxylin and eosin, $\times 30$).

Fig. 2. Benign leiomyoma of the stomach showing mature smooth muscle tissue in its characteristic arrangement. No mitotic figures are present (hematoxylin and eosin, $\times 30$).

Fig. 3. Highly malignant leiomyosarcoma of the stomach. Note the unduly growing, highly undifferentiated cells and the presence of mitotic figures (hematoxylin and eosin, $\times 34$).

Fig. 4. Hemangioendothelioma, or angiosarcoma, of the stomach. Notice how the endothelial cells, in an attempt to form new vessels, have arranged themselves into cord like structures some of which have already been cannalized and contain erythrocytes (hematoxylin and eosin, $\times 30$).

Fig. 5. Fibrosarcoma of the stomach. It has myxomatous changes (hematoxylin and eosin, $\times 30$).

In this series 8 of 14 patients, or 57.1 per cent, had one or more reasonably definite features of ulcer. These consisted of periodicity, epigastric pain coming on after meals, relief of pain after ingestion of food and alkali, nocturnal pain, and a history of previous roentgenological diagnosis of ulcer. The preoperative clinical diagnosis in 2 cases was peptic ulcer, while in 3 cases a roentgenological diagnosis of ulcer had been made previously.

Incidence Sarcoma has been estimated variously to comprise from 1 to 8 per cent of all neoplasms of the stomach. Ewing estimated its frequency at 1 per cent, while Fenwick expressed the opinion that it comprises from 5 to 8 per cent of all gastric neoplasms.

Age Sarcoma of the stomach affects all age groups, although the period between 40 and 60 years of age comprises the largest group. The youngest patient appearing in the literature is that reported by Finlayson, a child 3 years of age with a fatal outcome 6 months later. The oldest patient, 91 years of age, was reported by Di Giacomo.

The average age of patients who have gastric sarcoma is considerably less than that estimated for carcinoma. Douglas quoted the average age for gastric carcinoma from the United States census figures as 61.2 years.

In this series the average age of the patients was 43.2 years, the youngest being 10 years of age. Almost half of our patients fell in the age group of 40 to 50 years. In 11 of our 14 cases the lesion was leiomyosarcoma, the average age of the patients was 46.6 years. There were 2 cases of hemangioendothelioma, in which the patients were 10 years and 29 years of age, respectively. In the case of fibrosarcoma the patient was 54 years old.

Sex The average reports in the literature state that the sex is divided about equally, although such observers as Balfour and McCann, and Lunov and Zeller report a preponderance in males.

In our 14 cases 9 of the patients, or 64.3 per cent, were males and 5, or 35.7 per cent, were females. Only 3 of the 11 leiomyosarcomas were found in females while both of our cases of hemangioendothelioma were in males. The 1 case of fibrosarcoma occurred in a male.

PATHOLOGY

Attempts to classify sarcomas of the stomach pathologically have met with varying degrees of success. Seventeen different classifications have been encountered in the literature and these appear to have little uniformity.

It is apparent, therefore, that some simple inclusive classification should be decided on. It is recognized fairly generally that lymphosarcomas make up a definite class of gastric tumors, not only clinically and pathologically, but also in regard to their treatment and prognosis. The remaining types of gastric sarcoma, which comprise about a fourth of the total number, may be divided into three groups: leiomyosarcoma, hemangioendothelioma or angiosarcoma, and fibrosarcoma.

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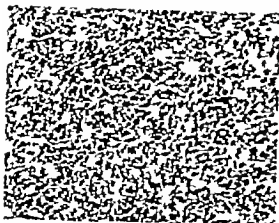


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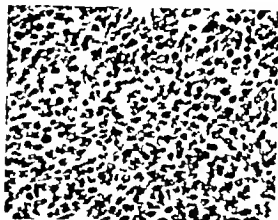


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these lesions are found most frequently arising from the lesser curvature of the stomach in which location they occurred 5 times. Other locations were encountered in the following order: posterior wall, 3 times; anterior wall, greater curvature, and pyloric end of stomach, each 2 times.

Gross characteristics. Sarcomas of the stomach vary considerably in their gross characteristics, depending on their cell of origin, location and rapidity of growth. Generally speaking they are fairly rapidly growing tumors with a tendency to grow expansively in the connective tissue and vascular framework of the organ rather than to grow by infiltration as is so common with carcinomas.

The types of sarcoma under discussion here usually are sharply limited from the surrounding normal tissue, although a true capsule usually is wanting. They are usually highly vascular and for this reason often reach an enormous size. One of the largest was that reported by Cantwell which weighed 13 pounds (5.4 kilograms).

Because of their rapid growth and great size attained, secondary changes are encountered frequently. Some of these such as edema, hemorrhage and mucoid degeneration, tend to increase the bulk of the lesion further. When the limit of growth is reached, as determined by the blood supply, infarction and necrosis occur. Infection may follow and often accounts for the febrile course seen in certain cases of gastric sarcoma. Degenerative cysts and abscesses likewise may form. Perforation is fairly common. Hesse stated that perforation occurs in 8 per cent of cases.

Ulceration of the mucous membrane occurs late in the course of the disease and is usually the result of pressure necrosis; the mucosa not being involved primarily in the growth. Hemorrhage occurs either in the gastric lumen or in the tumor itself as a result of ulceration and rupture or thrombosis of the blood vessels.

Leiomyosarcoma originates in the smooth muscle cells of the muscularis, is fairly slow growing, and usually is well demarcated from the rest of the gastric layers.

Hemangioendothelioma has its origin in the endothelial cells of blood vessels. Being a

connective tissue tumor it can be classed as a sarcoma. Growthy, it may simulate leiomyosarcoma and fibrosarcoma very closely and is usually well circumscribed, frequently pedunculated and but rarely infiltrating.

Fibrosarcoma of the stomach takes its origin from the wall most frequently in the submucosa. It rarely assumes the form of an infiltrating growth and usually remains as a well demarcated intramural tumor.

These types may remain confined to the stomach wall as intramural growths, but, more frequently, they grow inward or outward to form sessile or pedunculated endogastric or exogastric tumors. The exogastric is perhaps the most common form, and because of the relative ease of its surgical removal and its slowness to metastasize, it is considered less malignant than the endogastric or infiltrating forms.

Microscopic characteristics. The histological appearance of sarcoma varies considerably but usually resembles that of its tissue of origin. In the slower growing well differentiated tumors, little difficulty is encountered in diagnosis but, with increasing anaplasia, the form of their originating cells is lost and classification may be difficult. The cells themselves may be divided into two groups for all sarcomas of the stomach, namely, round cells and spindle cells. These may be subdivided further into small and large round cell or spindle cell sarcomas. These different cell types may be present alone or in combinations in any of the four types of sarcoma. As a rule, however, the round cells are confined to the lymphosarcoma type, while the spindle cells make up the leiomyosarcomas, hemangioendotheliomas, and fibrosarcomas.

The microscopic picture of leiomyosarcoma consists of immature smooth muscle cells of varying degrees of differentiation grouped into interlacing bundles and bands separated by a fibrous stroma whose amount depends on the compactness of the tumor structure. When of low grade malignancy (Fig. 1) these tumors appear very similar to benign leiomyomas (Fig. 2) and frequently one is mistaken for the other. The finding of mitotic figures, however, establishes the malignant nature of the lesion (Fig. 3).

Microscopically, hemangioendothelioma are composed of large oval or spindle shaped endothelial cells arranged in a manner attempting to form new blood vessels (Fig 4). These are very vascular tumors containing numerous blood spaces and sinuses filled with erythrocytes. Their cells are usually quite mature and therefore they are easily confused with benign hemangiomas. Here, again, the presence of mitotic figures establishes the diagnosis of malignancy.

The fibrosarcoma is made up of connective tissue cells varying in appearance from that of immature fusiform fibroblasts to that of almost mature fibrous connective tissue cells (Fig 5). The same general interlacing pattern is noted. The cells themselves usually are elongated, oval, or spindle shaped with large granular nuclei. Mitotic figures are always present.

Degree of malignancy. As in all types of malignant tumors, the degree of malignancy of these gastric sarcomas varies according to the proliferative activity and differentiation of their cells. As a general rule they are less malignant than lymphosarcomas, not only in regard to cellular proliferation but also because they are usually noninfiltrating, more or less circumscribed, and often pedunculated growths which are more easily extirpated surgically.

Metastasis. Metastasis has been estimated variously by different observers as occurring in from a third to three-fourths of all cases of gastric sarcoma.

Most authors agree that metastasis occurs most often in the regional lymph nodes of the stomach and in the liver. The liver was involved by secondary deposits at the time of operation in 3 cases, or 21.4 per cent, in this series. In each of these 3 cases the location of the metastatic deposits was noted as being in the liver, and in 2 of them, metastatic nodules were found in the omentum and peritoneum, respectively. In 1 of these inoperable cases, the involvement of the liver was not found until operation, the abdomen was closed after a specimen for biopsy had been secured from the tumor, which proved to be a hemangioendothelioma. More than 6 years later this same patient returned to the clinic

and exploration was performed again. Metastatic deposits were found again in the liver and, this time, also in the omentum. A biopsy was made which confirmed the first report, and no further surgical intervention was attempted. The patient died about 6 months after the last operation. In 2 of the operable cases metastasis was reported in the liver 6 years and 3 years, respectively, after operation, which brings the total known metastatic growths in the liver to 5 cases, or 35.7 per cent.

CLINICAL MANIFESTATIONS

The clinical manifestations of sarcoma of the stomach generally are considered indistinguishable from those of any other malignant or sometimes benign tumor of the stomach. The sarcomas are confused most often with gastric carcinoma, peptic ulcer, and benign bleeding gastric leiomyomas.

There are no definite pathognomonic signs, symptoms, or laboratory criteria on which a diagnosis of sarcoma of the stomach can be made before operation. Recognition of the malignant nature of the lesion, however, is the matter of prime importance, whereas the particular type of neoplasm is only of secondary consideration.

The onset of the disease, although usually insidious, may be sudden and the symptoms may vary from the mildest dyspepsia to the severest manifestations of gastric carcinoma.

The course of these tumors is relatively slow. In 1 of our patients, one or more gastric symptoms had been present for as long as 15 years, while $3\frac{1}{2}$ years was the average duration of symptoms before medical aid was sought here. The shortest period in which symptoms had been present was 4 months.

Symptoms. The symptoms which bring the patient to seek medical aid are not generally such early ones as mild dyspepsia, epigastric distress, nausea, and anorexia. Usually it is the onset of severe abdominal pain, a rapidly enlarging abdominal mass, hemorrhage from the growth in the form of melena or hematemesis, vomiting, or marked loss of weight which brings the patient to consult his physician. By this time, of course, the disease is well advanced and secondary complications often have occurred.

Pain, hemorrhage, vomiting, and the production of severe digestive disturbances occur late in the course of the tumor after it has invaded the mucous membrane or become large enough to produce pressure necrosis and ulceration of the mucosa. Following this, cachexia soon may become manifest. Most observers agree that it occurs at a later stage in this disease than it does in carcinoma. Pain was found to be the most frequent presenting complaint; it occurred in 13 of 14 cases, or 92.9 per cent.

Nausea and vomiting were second in order of frequency and were present in 8 cases, or 57.1 per cent. In only 3 of these or 21.4 per cent, did the patient give a history of hematemesis. In 2 of our cases the pylorus was involved in the growth but in only 1 of these did the patient complain of vomiting. No hematemesis had ever been noted in this case and the vomiting was not of the type usually seen in pyloric obstruction. Almost all observers agree that vomiting and hematemesis occur less frequently in sarcoma than they do in carcinoma of the stomach.

The presence of an abdominal tumor mass was the next most frequent finding occurring in half of our cases. In 5 of these the mass had been discovered by either the patient or his local physician before admission to the clinic. The shortest duration of the tumor was 2 weeks, the longest 9 years, while the average duration was more than 4 years. In all cases the mass was located in the upper part of the abdomen, usually the left part of the epigastrium, and in most cases was said to be movable.

Melena occurred in 6 or 42.9 per cent, of our cases, and was the fourth most frequent complaint. Its usual duration was a few months but in 1 case it had been present intermittently for 15 years. Both Reeves and Fenwick have called attention to the frequency of hemorrhage in their patients and the latter estimates that it occurs in 50 per cent of cases.

Weakness and pallor occurred in 4 cases and were attributed to the secondary anemia present. The average concentration of hemoglobin for these cases was 46 per cent (6 grams per 100 cubic centimeters of blood). The

erythrocyte count averaged less than 3,500,000 cells in each cubic millimeter of blood.

Indefinite digestive disturbances were complained of in 4 cases, or 28.6 per cent. These were variously referred to by the patient as "gas on the stomach," "heart burn," dyspepsia, or indigestion. In the majority of cases they preceded other symptoms of the disease and in 1 case they had been present for 24 years.

Loss of weight was recorded in 3 or 21.4 per cent, cases but was not striking. The loss of 35 pounds (15.3 kilograms) in approximately 2 years was the greatest decrease noted.

The remaining symptoms occurred in an occasional case and consisted of constipation, anorexia, fever and dizziness or fainting in order of frequency. The only significant ones in this group are fever, dizziness, and fainting. Fever, though not common, was present in 3 of our cases and represented secondary infection of the tumor or formation of abscess. Dizziness and fainting were noted in 2 cases and in each case they heralded a severe gastric hemorrhage which soon became manifest by hematemesis or melena.

The arrangement of the foregoing symptoms into an ulcer pattern was noted a number of times. This was suggestive enough in 3 cases to enable a preoperative diagnosis of peptic ulcer to be made.

In a few cases the only symptoms complained of by the patient were those resulting from secondary complications of the gastric tumor. Infection, formation of abscess, perforation of the stomach, peritonitis, and other complications present typical clinical pictures with their characteristic type of pain, febrile course, and other symptoms.

Laboratory methods of diagnosis. No laboratory criteria have been established by which a definite diagnosis of gastric sarcoma can be made. Roentgenological examination is the most satisfactory, however, and while the type of malignancy may not be determined by this method, the diagnosis of a malignant gastric tumor almost always can be made. Kirklin and Weber in discussing roentgenological diagnosis of neoplastic disease stated that sarcoma of the stomach is rare and

"although unmistakable roentgenological evidence of the malignant nature of the process usually can be elicited, the roentgenologist is prone, on account of its comparatively low incidence, to designate the process carcinoma rather than sarcoma."

Gastroscopy has been employed recently in an effort to diagnose gastric sarcoma before operation. Schindler expressed the opinion that this condition "may present a characteristic picture in the gastroscope which is entirely different from all other diseases of the stomach." In 1 of our cases a diagnosis of recurrent sarcoma of the stomach was made gastroscopically 2 years after surgical excision of the tumor.

In former years considerable importance was attached to gastric analysis in the diagnosis of these lesions. It was believed that the amount of free hydrochloric acid was normal or excessive in gastric sarcoma and, as we know, usually absent in carcinoma of the stomach. This was used as a point of differential diagnosis. In none of our cases in which the gastric analysis was reported was there complete absence of free hydrochloric acid. All had approximately normal free and total hydrochloric acid determinations with the exception of 1 case which was slightly higher than normal. Westphalen reported a case in which he made a diagnosis of gastric sarcoma by microscopic examination of a bit of tumor tissue obtained by gastric lavage.

It would seem, then, that in order to make a diagnosis of sarcoma of the stomach, the clinical picture and laboratory findings must be considered carefully as a whole and differentiated from those characteristic of other gastric lesions without too much reliance being placed on any one particular finding. Frazier summed up the picture well by saying, "in a patient presenting gastric symptoms of several months' duration with a readily palpable, freely movable tumor of the stomach but without loss of weight, general debility and cachexia common to carcinoma of the same duration, one might be justified in suspecting sarcoma."

Differential diagnosis In the differential diagnosis of leiomyosarcoma, hemangioendothelioma, and fibrosarcoma of the stomach,

the lesion which simulates them most closely, of course, is lymphosarcoma. In view of the fact that sarcoma is practically never differentiated clinically from other malignant and, in some cases, benign lesions, it would be absurd to attempt to establish criteria here by which specific types of sarcoma could be recognized clinically.

There are, however, a few differentiating characteristics which may be mentioned. Lymphosarcoma is likely to occur in younger persons, 30 to 40 years of age, is of higher grade malignancy and so runs a more rapid course with earlier metastasis than other types of gastric sarcoma. The pylorus is involved more frequently and, while it often remains unobstructed in spite of this, disturbances of gastric motor function are more common. A palpable abdominal mass is encountered less often. Involvement of the mucosa by infiltration occurs relatively early, resulting in earlier and more severe pain and greater tendency to gastric hemorrhage, infection, and perforation. Cachexia is more severe and earlier in its occurrence. There is more likely to be an associated enlargement of the spleen, and lastly, lymphosarcoma is highly sensitive to irradiation therapy.

Carcinoma is by far the easiest lesion to confuse with sarcoma of the stomach and in most instances is practically impossible to differentiate with any degree of accuracy. Certain differentiating features exist, however, but none is conclusive. Gastric carcinoma, as a rule, occurs late in life, the average age being about 60 years. It is a tumor of epithelial origin and consequently involves the mucosa first. Because of this, ulceration with its resultant hemorrhage, infection, and perforation occurs earlier and more frequently than in gastric sarcoma. Carcinoma is usually infiltrative and involves the pylorus in about 60 per cent of the cases. For this reason symptoms of pyloric obstruction and gastric retention are much more common. Carcinoma of the stomach is a much more rapidly growing lesion than sarcoma, is more malignant, runs a considerably shorter course, metastasizes earlier, and is accompanied by more severe systemic effects such as secondary anemia, emaciation, and cachexia. A palpable

abdominal mass is less likely to be encountered unless very late in the course of carcinoma and then it usually is fixed.

There remain so many lesions which must be considered and ruled out when arriving at a diagnosis of gastric sarcoma that it is impossible to give their distinguishing features here. Of these, benign gastric ulcers are probably the most important because of their frequent occurrence. Benign leiomyomas may simulate sarcoma if they attain considerable size. These are considered the most common tumor of the stomach by Rlenlets, who found them present in 16 per cent of routine necropsies. Other benign gastric lesions to be considered are pedunculated polyps and gastric syphilis.

Tumors and cysts of almost any of the abdominal viscera may be confused with gastric sarcoma. Splenomegaly especially that occurring in Banti's disease, in which associated gastric hemorrhages and secondary anemia are common is often difficult to differentiate from gastric sarcoma.

PROGNOSIS

The prognosis in all forms of gastric malignant neoplasia necessarily must be guarded and sarcoma is no exception to this rule. The particular type of sarcoma has a great deal of bearing however on the ultimate prognosis. It is accepted by most observers that the types discussed here namely leiomyosarcoma, hemangioendothelioma or angiosarcoma, and fibrosarcoma, offer the best prognosis.

W. J. Mayo stated that in his experience he was impressed by the longer course and better surgical results obtained in gastric sarcoma as compared with gastric carcinoma.

Hemangioendotheliomas offer the best prognosis of any of the gastric sarcomas. Clignozzi called attention to the chronic course of hemangioendotheliomas and maintained that symptoms develop gradually and are not pronounced until late in the course of the disease, and that emaciation and metastasis are absent. One of our patients was living and perfectly well when last heard from, 13 years after partial gastrectomy at the age of 10 years, for a hemangioendothelioma of the stomach.

The pedunculated form of gastric sarcoma offers a better chance of cure than the infiltrating type because it is more easily removed surgically and is usually one of the less malignant types. The diffuse infiltrating forms, almost always lymphosarcoma, are rapidly growing tumors and less amenable to surgical removal. For this reason they may offer even a worse prognosis than does carcinoma of the stomach.

In our group of 14 cases, comprising only leiomyosarcomas, hemangioendotheliomas and fibrosarcomas, 7 of the patients are known to be dead at the time of writing. Six patients were living when last heard from and 1 patient was lost track of soon after operation. Of the patients who have died the average duration of life after operation was 3 years and 4 months. In the 6 patients who were living when last heard from, the average duration of life following operation was more than 4 years.

TREATMENT

The treatment of sarcoma of the stomach, regardless of cell type is surgical. Leiomyosarcomas, hemangioendotheliomas and fibrosarcomas usually remain locally operable and without metastasis until rather late in their course. Counseller and Collins emphasized the fact that these tumors at first appear to be inoperable because of their size and the adherence to them of the greater omentum and viscera. They expressed the opinion, however that the sharp line of demarcation from normal stomach wall makes extensive resection possible. For this reason Balfour and McCann recommended abdominal exploration in spite of a roentgenological report of inoperability.

Glenn and Douglas claimed that sarcoma has a better operative prognosis as a group than carcinoma and that of sarcomas, leiomyosarcoma, hemangioendothelioma, and fibrosarcoma are more amenable to surgical measures than lymphosarcoma.

In our patients partial gastric resection was carried out in 8 cases, of which 5 were of the posterior Polya type, 1 was an anterior Polya resection, and 2 were segmental resections. Local excision of the tumor was done in 3 cases and 3 cases were simply abdominal explorations in which specimens for biopsy

re removed from inoperable tumors for microscopic diagnosis

Additional surgical procedures were performed in 2 cases. In 1 of these pyloroplasty was done in addition to the segmental resection. In another in which the tumor had been excised locally gastrostomy was performed and radium was inserted.

There were no postoperative deaths in our series of 14 surgical cases. The shortest duration of life following operation was 3 months. Only 1 case was any serious postoperative complication mentioned and this was bilateral bronchopneumonia from which the patient made a satisfactory recovery.

Aside from surgical intervention, irradiation offers the only method of treatment of sarcoma of the stomach. Its field is limited, however, and it rarely proves of value in sarcomatous lesions other than lymphosarcoma. Lymphosarcoma is highly sensitive to irradiation and Desjardins stated that early lesions of this type may be cured by irradiation alone. Repeated series of roentgen irradiation were used as an adjunct to operation in 2 of our cases, in 1 of which radium was also used as a supplement. In 1 of these cases the lesion was inoperable and the patient lived more than 6 years with metastatic growths present in the liver all the time. The other patient suffered a recurrence 2 years after operation.

SUMMARY

Fourteen histologically proved cases of gastric sarcoma, exclusive of lymphosarcoma and including 11 leiomyosarcomas, 2 hemangioendotheliomas or angiosarcomas, and 1 fibrosarcoma, in which operation has been performed at the Mayo Clinic between 1908 and 1938, inclusive, were studied clinically and pathologically.

An attempt has been made to simplify the terminology and classification of sarcoma of the stomach and to point out the clinical and pathological features distinguishing the leiomyosarcomas, hemangioendotheliomas, and fibrosarcomas as a group separate from lymphosarcoma.

CONCLUSIONS

The cause of sarcoma of the stomach is unknown. Evidence may be found pointing to

its origin in normal cells, congenital isolated cell rests, traumatized or inflamed tissues, benign tumors, and gastric ulcers. Males were affected in 64.3 per cent of our cases. The average age for the group was 43.2 years.

All sarcomas of the stomach may be classified into four types: lymphosarcoma, leiomyosarcoma, hemangioendothelioma or angiosarcoma, and fibrosarcoma. The last named three most often involve the curvatures of the stomach, more rarely the pylorus or cardia. They originate in the submucous or muscular layers of the stomach wall, are usually well circumscribed, are often pedunculated, and tend to assume an exogastric or endogastric form, although in rare cases, they may be infiltrating.

They may be composed of round cells or spindle cells, large or small, depending on the proliferative activity of the growth and the amount of cellular differentiation. Histologically the cells group themselves in a characteristic arrangement of interlacing bundles and whorls.

Leiomyosarcoma, hemangioendothelioma, and fibrosarcoma are usually of an average grade of malignancy. Metastasis occurs in about a third of the cases, the most common sites being the regional perigastric lymph nodes and the liver.

There are no pathognomonic clinical findings or laboratory criteria on which a definite diagnosis of sarcoma of the stomach can be made. The clinical and laboratory picture must be considered as a whole and the fact that the malignant nature of the lesion is recognized is the one of prime importance. The onset may be sudden or insidious. Symptoms usually appear late and the duration of symptoms before treatment averages $3\frac{1}{2}$ years. The chief signs and symptoms in their order of frequency are pain, nausea and vomiting, abdominal tumor, melena, weakness and pallor, digestive disturbances, hematemesis, and loss of weight. Frequently patients give a history suggestive of peptic ulcer. No laboratory procedures are considered definitely diagnostic, although roentgenographic examination usually establishes the malignant nature of the lesion. Carcinoma of the stomach offers the greatest differential diagnostic

problem. Other lesions to be considered are benign gastric tumors and ulcers and tumors or cysts of almost all the abdominal viscera.

The prognosis, while guarded is better than that of lymphosarcoma or carcinoma. Secondary complications, such as ulceration, hemorrhage, infection, formation of abscess, perforation, peritonitis, and metastasis, make for a much poorer prognosis. The particular cell type is a factor in the prognosis. The more mature the cells and the slower the growth, the better is the prognosis. There were no operative or immediate postoperative deaths among our 14 patients.

The treatment of choice is operation and it is the only treatment that has anything to offer in leiomyosarcoma, hemangioendothelioma, or fibrosarcoma. Lymphosarcoma responds readily to irradiation but this form of treatment is of little value in other types of gastric sarcoma.

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PNEUMONIA AS A COMPLICATION OF BILIARY COLIC

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ONE of us began to practice medicine more than 31 years ago, and almost immediately encountered cases in which the illness started as a frank attack of biliary colic and soon after developed into pneumonia. At the onset there was no fever, cough, dyspnea, or abnormal physical signs in the lungs. On the contrary, severe epigastric or right upper quadrant pain prompted the patient to seek help, the pneumonia came as an unpleasant surprise to us and to the patient's family. While the usual abdominal complications of biliary colic had been explained, we did not expect the complication of pneumonia which proved to be most annoying and at times even hazardous. About 20 years ago one of our patients, a middle aged woman, died of pneumonia although the coexisting gall-bladder attack had subsided. During the first 15 years, in a large general practice, no time or opportunity was afforded to study this problem. We kept no record of the cases, but there must have been 6 or possibly 9 during that period. The case referred to was the only one we can remember which terminated fatally. As a result of this experience we began to fear pneumonia more than the other better known complications, and it was always a source of amazement to us that neither the current medical literature nor discussions in medical societies made mention of this complication.

However, during the past 16 years we have had an opportunity to practice in a hospital, and this has given us a better chance to study such cases. Laboratory facilities were also thus available, in addition to knowledge obtainable from cases of other members of the staff. As a result of our study we have become convinced that our early impressions were correct.

A search of our hospital files for the years 1921 to 1940 revealed 11 instances which exemplify the complication here described. A number of other cases of biliary disease with

pneumonia were noted, but the histories failed to reveal the sequence of events described so they are not included here. Cases of postoperative pneumonia were properly excluded, although it seemed to us that in many instances the pneumonia probably existed before the operation.

CASE 1 No 108367 R G, female, aged 48 years. She had had an attack of biliary colic 4 years ago. On October 6, 1940, the patient was seized with an attack, in the right upper quadrant of the abdomen, of severe pain which radiated to the back. She vomited several times. An injection of morphine was given. The next day she had another similar attack, for which she again received morphine. The temperature was normal and the lungs were clear. The pain continued. She then began to cough a little, but there was no expectoration. On October 10 the patient was admitted to the surgical service of the Beth-El Hospital with a diagnosis of acute cholecystitis. The temperature on admission was 104 degrees F, the pulse was 120, and the respirations, 42 per minute. Bronchovesicular breathing and moist râles were heard over both lower lobes posteriorly, more on the right than on the left. The gall bladder was greatly enlarged, reaching almost to the iliac crest, and was very tender. The patient was transferred to the medical service. X-ray examination of the chest confirmed the clinical diagnosis of bilateral pneumonia. The white blood cells numbered 17,700 with 86 per cent polymorphonuclear cells. The blood culture was negative. Sul fapyridine was given, but was discontinued on October 14 because of the appearance of jaundice and bile in the urine. Oxygen was also given. The temperature came down to normal by October 12. On October 15 she had another attack of biliary colic which required morphine. Following this her temperature rose to 102 degrees F. On October 24 there was another rise in temperature following another attack of colic. The pulmonary signs gradually cleared up, but the gall bladder remained palpable. A flat plate of the gall-bladder region on October 20 revealed numerous gall stones.

It is noteworthy that although this patient was extremely ill she had only a slight cough and no expectoration at all. She refused operation and was discharged on November 4, 1940.

CASE 2 No 28542 L E, female, aged 60 years. Illness began on June 1, 1928, with pain in the right upper quadrant of the abdomen. On June 9 there

From the Medical Service, Beth El Hospital

was pain in the left lower chest. The next day the patient began to cough and expectorated bloody sputum. She was admitted to the hospital on June 3. The gall bladder was enlarged and tender and there was consolidation of both lower lobes more extensive on the left side. Two days later an x-ray examination of the lungs showed slight haziness of the left base. The temperature reached normal in 6 days, and the patient made an uneventful recovery.

CASE 3. No. 86. R. H., female, aged 36 years. This patient gave a history of repeated attacks of biliary colic with jaundice extending over several years. Her present illness began on August 6, 1930 with a typical attack of biliary colic. On August 10 she began to cough, and the temperature rose to 101 degrees F. She was admitted to the hospital on the following day with a large tender gall bladder and with pneumonia of the right lower lobe. The patient made an uneventful recovery.

CASE 4. No. 8560. Z. C., female, aged 47 years. One year before admission to the hospital the patient had a typical attack of biliary colic. Her present illness began on August 13, 1937 with diarrhea, chills, fever and headache. 24 hours later she developed severe abdominal pain which became localized to the right upper quadrant of the abdomen. Morphine was administered. Two days later she was admitted to the hospital. The gall bladder was enlarged and tender; the lungs were clear. Three days later there was a definite pneumonia of the left lower lobe and 4 days after that the right lower lobe also became involved in the pneumonic process. An x-ray film confirmed the diagnosis of bilateral pneumonia. The gall bladder increased in size reaching almost down to the iliac crest, and the leucocyte count rose to 15,000, with 80 per cent polymorphonuclear cells. An operation was advised. However the patient refused operation and signed herself out of the hospital on August 26. (We learned later that the symptoms gradually subsided and the patient got well, without operation.)

CASE 5. No. 66907. A. A., female, aged 70 years. The patient had an attack of biliary colic 6 years ago and another attack 3 months ago. The present illness began on April 20, 1939 with pain in the right upper quadrant of the abdomen. On examination large, tender gall bladder was found. On April 25 she was admitted to the hospital. In addition to the large gall bladder a lag of the right chest was noted, and a few rales were heard at the right base. Within the next few days she developed a full-blown pneumonia involving the entire right lung and the left lower lobe. This was confirmed by an x-ray film of the chest. There was very little cough and no sputum. The patient made an uneventful recovery and left the hospital on May 5, 1939.

A search of the literature pertaining to this subject revealed very little. Neither text

books on general medicine nor special books on the gall bladder make mention of pneumonia as a complication of biliary colic. The most recent book on this subject (6) published in 1940 discusses at great length the various complications of biliary disease but entirely omits pneumonia. Carter Greene and Twiss describe impairment of resonance and diminution of breath sounds due to elevation of the diaphragm secondary to sub-diaphragmatic pathology. Wilkie states that due to the "rigidity of the right half of the diaphragm, as proved by x-ray examination, the picture may therefore resemble a primary right-sided lung affection. The chill at the onset, the thoracic pain, the catch in the breathing combined with the fact that owing to the immobile diaphragm and deficient expansion of the right base crepitations are frequently to be heard on auscultation all these features may divert attention from the abdomen to the chest. Many of my patients gave a history of previous attacks diagnosed as congestion of the lung. The pulmonary signs should always be looked for and assessed at their true value. In 1912 Babritt (2) described cases of obscure fever with the physical signs of pneumonia either in the right or left, or in both bases, without the symptoms or signs of gall bladder disease. The fever subsided but frequently recurred. Eventually gall-bladder tenderness, or perhaps icterus, developed and the diagnosis of gall bladder disease became evident. He thinks that the gall bladder was the cause of the infection. His cases ran a protracted but mild course. However they differ from ours, because ours began as frank attacks of biliary colic without any signs or symptoms of pneumonia. The following case is an example of the type described by Babritt.

CASE 6. No. 82995. A. S., female, aged 60 years. The patient gave a history of repeated attacks of biliary colic. Cough and expectoration were also present for many years. The present illness began March 1937 with fever, cough and expectoration. She was admitted to the hospital on March 20. Her temperature was 101 degrees F, pulse rate 6 respirations per minute. X-ray examination revealed pneumonia of the right lower lobe. Tenderness in the right upper quadrant of the abdomen was noted on admission, but this was over

shadowed by the pneumonic symptoms. On March 22, jaundice developed and the gall bladder was found to be enlarged. The patient made an uneventful recovery.

This case makes us speculate whether a more careful history might not have revealed symptoms of biliary colic preceding the pneumonia.

In 1929, Akaiwa and Ishida reported 7 cases, a few of which are good examples of the type described by us. They called attention to the fact that "lung and bronchial inflammations very often follow biliary tract infections."

ETIOLOGY

The exact mechanism which operates to bring about inflammation of the lungs in gall-bladder disease is not known. Moreover, inflammations of other abdominal organs are also frequently complicated by pneumonia. We can recall a number of instances of pyelitis and pyelonephritis in which this complication arose. We were frequently at a loss to explain the fever of long duration by the renal infection alone. A careful examination of the lungs revealed the pneumonia. When this cleared, the fever subsided. Furthermore, it is very likely that the factors which are responsible for the production of pneumonia after abdominal operations are also responsible for the pneumonia that follows intra-abdominal inflammations. Intra-abdominal infection is commonly present in both cases. Also, spasm and elevation of the diaphragm and the shallow breathing induced by morphine are present in both conditions. Pulmonary atelectasis and bronchopneumonia may then ensue. The recumbent posture makes proper feeding difficult and tends to bring about aspiration pneumonia. Waters made "An attempt to reduce to a common denominator the etiological factors involved in the production of pulmonary complications," and came to the conclusion that, "with rare exceptions, such morbidity follows a period of interference with the normal functions of the respiratory mechanism, whether due to drug action, trauma, or illness."

Direct extension of the infection through the diaphragm to the lungs is a possibility, Kehling and Kehr, according to Akaiwa and

Ishida, favor this idea. However, there is no proof that this really takes place. One of Bahrdt's (3) cases came to autopsy 13 years after the pneumonia, no pathological changes were found in the right diaphragm, pleura, or lung. Akaiwa and Ishida injected pneumococci and staphylococci into the gall bladders of dogs, and succeeded in producing acute pneumonitis in some of the animals, provided the organisms were virulent and the common bile ducts were tied off. They think that the infection spreads through the blood stream. This is also Bahrdt's (3) opinion. If this were so, we would expect to find an equal distribution in all lobes. Actually, in our 11 cases as well as in those of Bahrdt and Akaiwa and Ishida, we found that although the lesion was usually bilateral, it was almost always confined to the lower lobes, with the right side predominating both in frequency and extent. In 7 of our 11 cases the lesions were bilateral, 3 involved the right lower lobe only, and 1 the left lower lobe only. While we realize that the number of cases is not sufficiently great to be significant statistically, this distribution suggests that no single factor can satisfactorily explain this complication.

CLINICAL FEATURES

One of the features which struck us particularly in these cases was the almost complete absence of cough and expectoration in most of the patients. We have no explanation for this. All 11 of the patients were females, varying in age from 29 to 70 years, with an average of 54.1 years. The interval between the onset of the biliary colic and the pneumonia was usually from 2 to 6 days, but in a few cases it was as long as 2 to 3 weeks. The white blood cell count varied from 8,400 to 21,000 (average 13,200), with from 71 to 92 per cent polymorphonuclear cells (average 83 per cent). Blood culture was done in 3 cases and was negative in each instance. Sputum typing could not be done in most of the cases because of the lack of sputum. All of the patients recovered. This we feel is noteworthy in spite of the smallness of the series, because of the advanced age of most of the patients, and the fact that they were suffering from two severe acute illnesses at the same

STUDIES IN DIETHYLSTILBESTROL

II Differences In Response of Radium Induced and Physiological Menopause

III Effect on Liver

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THE need for an effective estrogenic substance that does not require parenteral administration appears to have been met with the synthesis of diethylstilbestrol (4,4'-dihydroxy- α -beta diethylstilbene). This compound was developed in 1938 by Dodds, Goldberg, Lawson and Robinson who showed it to be active in oil, alcohol, water and as the acetate. They found it to be two to three times as potent as estrone under similar conditions. It bears no chemical relationship to estrone since it possesses no phenanthrene ring, but it produces almost identical physiological effects. The only biological differences that were observed were that stilbestrol has an appreciably less stimulating action on the mammary tissue than does estrone (5) that though stilbestrol like estrone will inhibit comb growth in capons when injected simultaneously with androsterone, it does not inhibit comb growth when applied to the comb by intunction (9, 10). This latter phenomenon has not yet been explained. However percutaneous absorption does occur and estrus can be produced in spayed mice whose necks are painted with stilbestrol in oil (10). Palmer and Zuckerman further showed that it was absorbed through the vaginal mucous membrane of spayed mice causing estrus to supervene.

The action and the effect of this synthetic estrogen on the human has been the subject of reports in Europe (16) and in this country (2, 7, 15). The reports all agree as to its effective use in producing clinical improvement in the symptoms of the menopause and in producing biological changes similar to those obtained with parenteral estrone or

estradiol but they vary in their evaluation of the development of undesirable side effects. It is with justifiable trepidation, therefore that this product was employed in preliminary studies and that its unqualified recommendation for general use was held in abeyance. Our study on several groups of patients, supplemented by laboratory observations, is presented in the hope that more information may be gained concerning the manner of its action and that a better evaluation of its indications and manner of administration may be secured.

METHODS EMPLOYED

The stilbestrol was administered orally in varying doses to two groups of women. One group consisted of patients who were suffering from the menopause syndrome and the other of postpartum women in whom large doses of stilbestrol were employed in order to observe its efficacy to inhibit or stop lactation. The latter group is discussed in a subsequent communication. The first group consisted of 28 menopause cases, 10 of which were radium induced, 11 surgically produced and 7 physiological cases. The subjective symptoms of each were observed before treatment was instituted and a definite routine was followed in the course of the study. It was believed desirable to study the three types of menopause cases separately since it had been our experience that radium induced cases were generally more refractory to treatment and because such patients required considerably larger doses in order to be controlled. The patients were seen at weekly intervals for a period of 4 to 5 months. During their visits vaginal smears were done and interpreted according to the criteria of Papanicolaou and Shorr. Endometrial biopsies were performed before treatment was

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TABLE I—SIDE EFFECTS OF STILBESTROL

	No of patients	Nausea	Vomiting	Breast pain	Abdominal or pelvic pain	Muscle cramps	Skin eruptions	Pruritus vulvae	Daily dose mgm	Relief of menopausal symptoms—%	Bleeding response
lum menopause	10	6	5	1	8	3	1	4	2-3	100	3
gical menopause	11	6	5	3	8	0	0	1	0.1-1.0	100	
siological menopause	7	4	1	0	6	2	0	3	0.1-1.0	100	6
al side effects	18	16	11	4	22	5	1	8			
al recoveries		13	11	4	10	5	1	7			

eks after treatment was started, and finally weeks after beginning the administration of stilbestrol. Urinalyses were done and the patients' subjective complaints tabulated regularly. The degree of amelioration of the menopause symptoms was observed during treatment, and the development and duration of toxic disturbances were noted simultaneously.

The radium treated patients had suffered from a bleeding dysfunction and varied in age from 42 to 50 years at the time that the radium was inserted. Previous to the radium treatment, diagnostic endometrial curettements had been done in order to rule out the possible existence of malignancy. These curtings served as a means of comparing subsequent endometrial biopsies that were secured after a period of treatment with stilbestrol. The patients were given 3 milligrams of stilbestrol daily by mouth so that a total of 14 milligrams had been administered in 5 weeks. Using a Meig's curette to secure endometrial biopsy tissue after 2 weeks' treatment, only 4 patients yielded sufficient material for examination. After 5 weeks' treatment, 8 of the 10 radium cases studied yielded enough material for examination. The 2 other patients exhibited complete closure of the external os, thus preventing the introduction of the curette. All the cases thus studied showed a proliferative nonsecretory endometrium which tended to duplicate in every way the picture of the endometrium before the radium was inserted. The modifying effect of the radium on the response of the endometrial glands, stroma, and myometrium to the stilbestrol was quite interesting and has been reported elsewhere (6). After the maximum

biological effect of stilbestrol was observed, the patients were maintained on treatment for a total period of from 3 to 4 months, during which time each had received approximately 324 milligrams of the drug.

OBSERVATION OF CLINICAL EFFECTS

In the hope that the side effects of the stilbestrol might be reduced to a minimum, it was decided to employ smaller doses at the beginning of treatment. Whereas 2 to 3 milligrams of stilbestrol were given daily to the radium induced cases, only 0.1 to 0.3 milligram was given daily to the surgical castrates and to the physiological menopause cases. The dose was then gradually increased. With the exception of vomiting, this did not appear to make an appreciable difference in the number of undesirable side effects that were experienced. Reference to Table I shows the range of undesirable or toxic symptoms experienced by our patients as well as the percentage of improvement. In all cases the well known symptoms of hot flushes, irritability, depression, and lassitude were either eliminated or so much relieved that they could be regarded as complete recoveries. Several patients who had received previous treatment with natural estrogens in single doses of 10,000 international units volunteered the information that the stilbestrol was much more effective and gave them a more pronounced feeling of well-being. This was especially true in the radium induced cases. The type of menopause apparently did not influence the development of toxic symptoms, though considerably more stilbestrol was necessary to control the menopause symptoms in the radium cases than for the physiological and surgi-

TABLE II.—INFLUENCE ON ENDOMETRIUM AND VAGINA IN RADIUM INDUCED CASES

	Spinal reaction	Atrophic vaginitis	Endometrial atrophy	Secondary amenorrhea	Stiff cervix	Stiff vagina
Before radium	Not taken					
After radium	Menstrual tumor	2				
5 weeks treatment (50 mgm.)	No response					
5 weeks treatment (15 mgm.)	responded					

cal types. With the exception of 3 of the 16 patients who complained of transient nausea and 11 of the 22 patients who stated that the recurring abdominal pain persisted all toxic symptoms disappeared as the treatment progressed. Five patients complained of intermittent cramps in the calf and thigh muscles and one patient experienced this discomfort in the muscles of the forearm. The cramps occurred chiefly during the night while the patients were lying down or during sleep, causing the patients to be awakened. It would also occur at times when arising in the morning. Fifty per cent of the radium induced cases experienced vomiting early in the course of treatment while only 14 per cent of the physiological cases were thus affected. This can be explained by the fact that the radium treated patients received 10 to 30 times as much stilbestrol as did the physiological cases. The only reference to the drug's effect on muscle was that made by Dawson and Robson whose studies were limited to its inhibitory influence on smooth muscle. No reference to its effect on skeletal muscle was found. None of the patients who experienced the undesirable side effects considered the discomfort sufficient to discontinue the drug. It is interesting to observe that none of the postpartum patients who were given large daily doses (5 to 10 mgm.) suffered side effects.

The proliferative endometrium produced by stilbestrol apparently results in bleeding which may (17) or may not (6) be regarded as a type of so called "withdrawal bleeding." All of our patients were treated without a rest period and we are therefore reluctant to consider the bleeding that ensued following treat-

ment for variable periods of time as due to sudden deprivation. Six of the 7 cases of the physiological group bled when a total dose of 90 to 100 milligrams was administered over a period of 4 to 6 weeks. Of the radium treated patients only 3 of the 10 showed bleeding during treatment extending over a period of 4½ months. In all cases in which bleeding occurred it began after treatment was in progress for approximately 6 weeks. We consider the fact as being of significance that bleeding ensued regardless of whether or not we employed the "deprivation method," especially since bleeding occurred in 86 per cent of the physiological cases but in only 30 per cent of the patients in whom the endometrium had been exposed to the effects of radium. Discussion of this fact will be taken up later.

LABORATORY STUDIES

The important laboratory studies concerned themselves chiefly with the vaginal smear, endometrial biopsies (Table II) and liver function tests (Table III). The potent biological effect of stilbestrol as mirrored by the vaginal smear method and the stimulation of the endometrium to proliferation has been amply observed (5, 10, 15). Our experience with but one exception, is in agreement with those of other workers in the field. The exception observed was a distinct difference in the time of biological response in the radium cases as compared to the physiological and surgical cases. It has been generally observed that vaginal epithelial and endometrial response occur after 2 milligrams of stilbestrol has been administered daily for a period of 10 to 2 weeks. This occurred in those patients in whom no irradiation had been employed. The patients treated with radium gave no endometrial or vaginal epithelial response after 2 weeks treatment. At the end of 5 weeks treatment a proliferative endometrium was observed and definite vaginal smear response took place. The physiological and surgical patients showed no such tendency toward a refractory state.

STUDIES OF THE EFFECT ON LIVER

During the course of the study we were especially concerned with the effect of stil-

bestrol on the liver In view of the moot question as to whether there is an impairment of liver function in consequence of treatment, 2 different liver function tests were performed on each of 14 patients and a single test on each of a group of 9 patients The bromsulphthalein test (13) was done 6 to 8 weeks after treatment was initiated and again 9 weeks after treatment was started Cognizant of the limitations of any single test as an indication of hepatic function, we supplemented this test with the hippuric acid synthesis test of Quick at intervals of between 3 and 5 months When the dose of stilbestrol was not very large, the hippuric acid synthesis test alone was employed The results obtained by Shorr and others who performed preliminary tests, indicate that the discrepancies observed in the hippuric acid synthesis test cannot be explained on the basis of resultant liver damage Ten patients showed an excretion of hippuric acid of less than 3.0 grams in 4 hours Of this number only one showed an excretion of less than 2.0 grams The 9 others were within a range of 2.5 grams It would be hazardous to suggest that this slight decrease can be interpreted as indicating liver damage, especially since it has been observed in some cases (15) that the hippuric acid synthesis shows improvement following administration of stilbestrol No retention of the bromsulphthalein was observed at the end of one-half hour in any of the cases studied As a result of our analyses it appears that the employment of stilbestrol in physiological doses gives no evidence of demonstrable liver damage in the human

STUDY OF THE EFFECT ON DOG'S LIVER

The important consideration regarding the possible toxicity of diethylstilbestrol concerned itself with the effect of this drug on the liver Aware of the limitations of present methods of evaluating liver function in the human, we turned our attention to the possible development of some anatomical (histopathological) disturbance as a result of its use Twelve full grown dogs were employed in the study The dogs were raised in our own laboratory and all had been on a standard ration since birth They were divided into 3

TABLE III—LIVER FUNCTION TESTS¹

Name	Bromsulphthalein test		Hippuric acid test Sodium benzoate	
	Date	Retention	Date	Excretion— gm
A O	12-4-39 1-5-40	½ hr 5% ½ hr 3%	1-30-40	3.1
L K	12-5-39 1-5-40	½ hr o ½ hr o	2-23-40	2.4
N B	1-3-40	½ hr o	2-23-40	2.4
A C	12-4-39 1-3-40	½ hr 4% ½ hr o	2-28-40	2.9
M.Z	12-4-39	½ hr o	2-29-40	3.1
A G	12-5-39 1-5-40	½ hr o ½ hr o	3-1-40	2.4
L Y	12-4-39 1-3-40	½ hr o ½ hr o	3-11-40	1.9
J P	12-5-39	½ hr o	3-12-40	3.01
A C			3-25-40	2.68
M.E.			3-6-40	2.96
V M			3-26-40	3.27
M D	1-4-40	½ hr o	3-27-40	3.3
A.P			3-28-40	4.2
E W			3-29-40	2.58
A K.			3-29-40	2.77
M.P	1-5-40	½ hr o	4-3-40	3.31
S J	1-3-40	½ hr o	4-4-40	3.17
B McA	12-4-39 1-5-40	½ hr o ½ hr o	4-5-40	2.03
R.K.			4-5-40	2.45
M J			4-2-40	2.95
H.B	12-5-39 1-4-40	½ hr o ½ hr Tr	4-8-40	3.3
F McK	1-4-40	½ hr o	4-9-40	2.16
M.S	12-5-39 1-5-40	½ hr o ½ hr o		

¹ Treatment started in each case October 30 1939

groups of 4 each, the sexes being equally divided The first group received 5 milligrams of stilbestrol dissolved in oil which was injected intramuscularly daily The second group received 10 milligrams daily, and the third group served as a control Treatment was continued for approximately one month—from November 29, 1940 to December 24, 1940 It should be observed that weight for weight, the amount of stilbestrol administered to the dogs as compared to the average human

dose was approximately 6 times as large. At the end of the injection period the dogs were anesthetized with nembutal and biopsy specimens of the liver were obtained.

Microscopic examination failed to show any difference between the livers of the treated dogs and those of the controls. These findings indicated that if a deleterious effect were present as a result of the use of diethylstilbestrol it was not reflected microscopically in the liver.

EVALUATION OF STUDY

Response of the uterus and vaginal epithelium to treatment in the menopause patient varies with their ability to be influenced by the drug. When physiological involution has occurred, stimulation can be readily accomplished with the natural and synthesized estrogens. Radium induced menopause presents a decidedly different problem due to the type of injury resulting from its use. The radium treated patient affords an excellent means of evaluating the potency of an estrogenic substance. Stilbestrol, by mouth was found to be effective in radium treated patients who had been refractory to previously employed parenteral preparations.

The differences in response to treatment between the physiological cases and the radium induced menopause are several. It required a longer period of preliminary treatment and the use of a dose five times as large to secure a satisfactory clinical response as well as comparable endometrial and vaginal epithelial change, as determined by biopsies and smears, in the radium treated patients as in the physiological cases. In addition to this, it is striking that only 30 per cent of the radium treated patients experienced vaginal bleeding while it occurred in 86 per cent of the physiological cases. In 2 of the 3 radium cases that had vaginal bleeding the duration was $\frac{1}{2}$ to $\frac{1}{3}$ days and was extremely scanty. In all of the physiological cases patients showed more profuse and extended periods of bleeding. An explanation of this observation lies in the effect of the radium on the uterus as reported by us (6) previously. The radium produces a marked degree of hyalinization of the stroma and portions of the myometrium as well as tending to destroy practically all of the gland

ular structures. There is an associated endarteritis with a consequent interference in capillary permeability. It may be this latter condition which accounts for the diminished bleeding response that is observed in the patients treated with radium.

We limited our studies of toxicity of stilbestrol to clinical evaluation assisted by liver function tests. The knowledge that the natural occurring estrogens are metabolized in the liver centered most of the attention on that organ. Our animal studies were chiefly concerned with the possible acute toxic effects on the liver. As previously mentioned we were unable to demonstrate any lesion in our treated dogs. Russell and co-workers recently reported their findings of chronic toxicity studies with stilbestrol. Employing rats, they found no pathological lesions in any of the organs save for an instance of cloudy swelling of the kidneys, although 5 times the average human therapeutic dose was used. When 26 times the therapeutic dose was employed, cloudy swelling of the kidneys was found to be present in 4 of 49 rats treated. Gastric hemorrhage and hemorrhage into the adrenals were observed in 1 animal. More extensive damage was reported when doses 323 times the human therapeutic dose were employed. It would apparently be the height of folly to condemn a drug because doses of such magnitude produced untoward effects. Morrell recently reviewed all of the clinical reports in this country and abroad and found no permanent toxic effects as evidenced by liver function tests, blood and urine chemistry and histological examination of the blood and bone marrow.

CONCLUSIONS

1. Diethylstilbestrol was employed to observe the differences in response to treatment of physiological menopause cases and radium induced cases. Its influence on liver function was also studied.

2. Radium induced menopause patients require larger doses and more prolonged treatment with stilbestrol than do physiological cases.

3. Bleeding response to treatment occurred in 86 per cent of the physiological cases and in only 30 per cent of the radium induced cases.

4 The undesirable side effects of stilbestrol are transient and are not sufficient to act as a deterrent to its use

5 Liver function tests and histological studies of dogs' livers failed to show hepatic damage after excessive doses of stilbestrol

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A STUDY OF THE MECHANICS OF BILE FLOW

II Responses to Intraduodenal Solutions

DONALD D KOZOLL, M.D. and H. NECHELES, M.D. Ph.D. Chicago, Illinois

In a previous paper we presented a method for simultaneous observation of the responses of the three factors we considered most important in determining the flow of bile, namely the contractility of the gall bladder the resistance of the sphincter of Oddi, and the tonus and motility of the duodenum. We confirmed the repeated observations of others on the independent activity of the sphincter and duodenum. In addition we reported our observations on the influence of physiological intravenous solutions on these structures (13).

Using the same experimental procedure on anesthetized dogs, we have studied the effects of various solutions introduced into the duodenum through a glass cannula which, projecting beyond the recording balloon, was tied around the cannula. All solutions were retained within the duodenum for a uniform length of time (2 minutes).

Intraduodenal instillation of 20 cubic centimeters of fresh gastric juice procured from dogs with Pavlov pouches of 1:12 to 1:14 1/10 normal hydrochloric acid concentration was observed on 13 occasions in 10 dogs. In every instance not complicated by previous medication an immediate marked elevation in sphincteric pressure coincident with a marked duodenal spasm was elicited both persisted for a considerable length of time after the juice had been permitted to drain out of the duodenum (Fig. 1). The gall bladder usually showed no characteristic response but in 2 instances there was a slightly increased tonus associated with an increase in motility. Blood pressure frequently revealed a 10 to 15 millimeter drop immediately following the injection.

Injection of similar amounts of tenth normal hydrochloric acid into the duodenum was followed by identical responses, although our gastric juice was slightly more acidic. Oddi, in his original work, stated that dilute hydrochloric acid caused a spasm of the sphincter but later work has been contradictory (5, 8, 9, 18).

Antispasmodics, such as atropine and transtentil, did not prevent the effect of gastric juice (refer to previous paper Fig. 4). No significant changes in gall-bladder tone or motility were observed following intraduodenal administration of hydrochloric acid or gastric juice. This is contrary to the experience of others (9, 18) but agrees with that of Bainbridge and Dale.

Twenty cubic centimeters of 1/20 normal sodium hydroxide instilled into the duodenum of 3 dogs, produced marked responses in each case. These were characterized by sphincteric spasm producing a prolonged rise in intraductal pressure (100 mm. and above). The duodenum responded with a marked increase in tonus and motility which did not always parallel the change of the sphincter resistance. The gall bladder showed no characteristic response, the blood pressure was unaffected, but this solution frequently produced hyperpnea (Fig. 3). These findings are consistent with the work of others (1, 5, 9). It is to be noted that sodium hydroxide produces much more marked and prolonged spasm of the duodenum and the sphincter than does hydrochloric acid of the same strength.

Injection of 5 to 10 cubic centimeters of a 1:1000 solution of peppermint water into the duodenum produced marked responses in practically all of 5 animals in which it was used. This agent produced a sphincteric spasm amounting to as much as 100 millimeter increase in intraductal pressure which frequently preceded and was out of proportion

From the Department of Gastro Intestinal Research, Michael Reese Hospital.
A preliminary report was read at the meetings of the American Physiological Society, April 19, 34, Chicago.
Dr. Kenneth Bernard Porter Research Fellow in Surgery

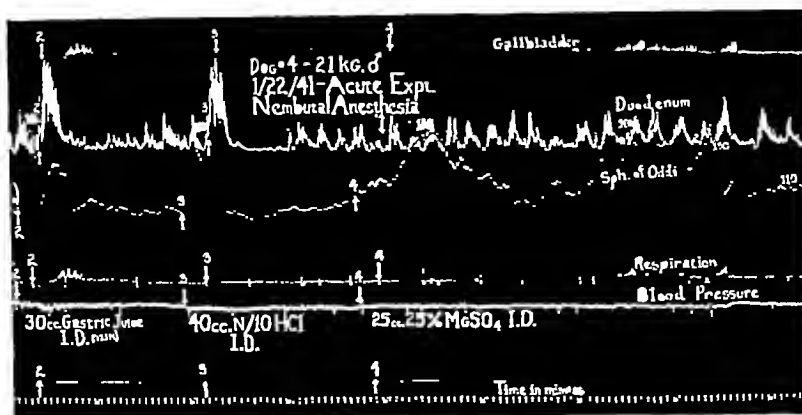


Fig 1 At 2, gastric juice intraduodenally, produced a concurrent spasm of sphincter and duodenum, but a recurrent sphincter spasm was not associated with further duodenal response. At 3, 1/10 normal hydrochloric acid had a similar effect. At 4, magnesium sulfate, intraduodenally, produced marked sphincter spasm with little effect on duodenal tone.

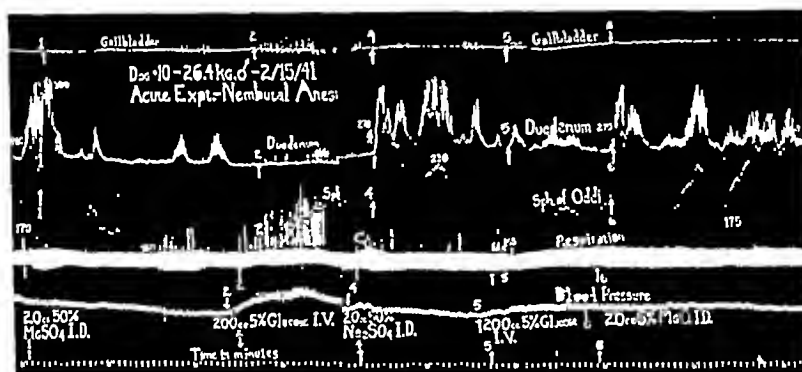


Fig 2 At 1, magnesium sulfate, intraduodenally, produced an initial marked spasm of sphincter (130 mm increase in pressure) coincident with duodenal spasm. Subsequently there was a lowering of sphincter tone below the control level, whereas duodenal tone and motility was restored to normal. At 2, glucose, intravenously, produced a 50 millimeter gradual rise in sphincter pressure, while depressing duodenal activity. At 4, disodium sulfate, intraduodenally, produced similar effects as did magnesium sulfate. At 5, isotonic glucose, intravenously, again raised sphincter pressure while depressing duodenum. At 6, magnesium oxide intraduodenally, produced marked recurrent spasms of sphincter which were coincident initially with duodenal spasms, but later were independent of it.

to a duodenal increase in tonus and motility. This effect is quite surprising in view of the fact that peppermint water is a time honored carminative. There was no effect on the gall bladder.

Twenty cubic centimeters of fresh dog's gall-bladder bile, introduced into the duodenum, produced no effect other than the transitory mechanical effect due to distention of the duodenum (Fig 3). As control, 20

cubic centimeters of normal saline was given, with similar negative results.

Twenty cubic centimeters of 25 per cent peptone solution, injected into the duodenum caused a moderate increase in sphincteric resistance and duodenal activity, which was of relatively short duration, and no gall-bladder response (Fig 3). Peptone has been described as a cholagogue secondary in effectiveness to egg yolk (1, 18).

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Using the same experimental procedure on anesthetized dogs, we have studied the effects of various solutions introduced into the duodenum through a glass cannula which, projecting beyond the recording balloon, was tied around the cannula. All solutions were retained within the duodenum for a uniform length of time (5 minutes).

Intraduodenal instillation of 20 cubic centimeters of fresh gastric juice procured from dogs with Pavlov pouches of 1:12 to 1:14 1/10 normal hydrochloric acid concentration was observed on 13 occasions in 10 dogs. In every instance not complicated by previous medication, an immediate marked elevation in sphincteric pressure coincident with a marked duodenal spasm was elicited both persisted for a considerable length of time after the juice had been permitted to drain out of the duodenum (Fig. 1). The gall bladder usually showed no characteristic response but in 2 instances there was a slightly increased tonus associated with an increase in motility. Blood pressure frequently revealed a 10 to 15 millimeter drop immediately following the injection.

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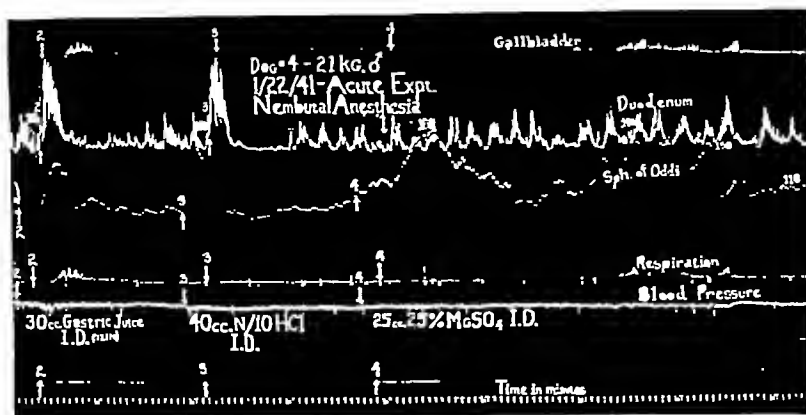


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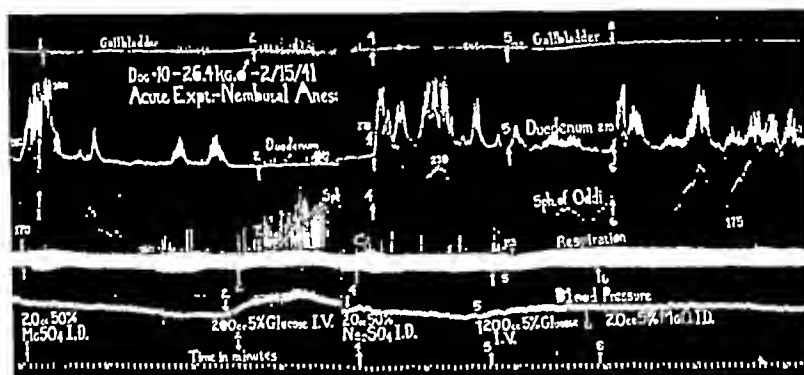


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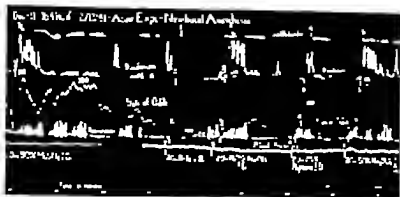


Fig. 3. At 2 magnesium sulfate intraduodenally produced an initial 90 millimeter rise in sphincter pressure coincident with duodenal spasm. Subsequently prolonged rise in sphincter pressure occurred, while duodenal tone and motility were low. Note relaxation in tone of gall bladder. At 3, intraduodenal injection of bile had only mechanical effect on the duodenum. At 4, 1/50 normal sodium hydroxide, intraduodenally produced simultaneous spasm of sphincter and duodenum. At 5, subsequent responses. At 4 peptone solution, intraduodenally produced moderate coincident spasm of duodenum and sphincter. At 5 dioxotic sulfate had similar effects as 1/50 normal sodium hydroxide.

Twenty cubic centimeters of a 25 to 50 per cent solution of magnesium sulfate was injected into the duodenum, and produced variable responses in 6 dogs in which it was used. The literature on magnesium sulfate has been completely reviewed by Ivy and our results reflect similar variabilities in the response to this drug. The drug is known to have an effect in the dog which is quite different from that which is supposed to occur in the human. In all animals this agent invariably produced an initial marked increase in sphincteric tone and duodenal activity (Figs. 1, 2 and 3). After this initial response in some animals there is a decrease in sphincteric and duodenal tone below that of what it was prior to injection (Fig. 2) whereas in others the sphincteric tone rises again in spite of the fact that the duodenum remains quiescent (Fig. 2 and 3). Particular attention is called to the occurrence of waves of spastic contraction of the sphincter of Oddi without similar response on the part of the duodenum. No effect was noted on the gall bladder except in one animal in which lowering of gall-bladder tone occurred parallel to the rise of intraductal pressure and lowering of duodenal tone (Fig. 3). This is the converse of the reciprocal effects on the gall bladder and sphincter attributed to magnesium sulfate by a number of observers (3, 10,

14, 15, 16, 17). Auster and Crohn quote work that proves that magnesium sulfate contracts rather than relaxes smooth muscle and that the local effect upon the duodenal obscures the effect on the sphincter. Doubt as to the consistent reciprocal effect of magnesium sulfate has been expressed (1, 5, 7, 19). Ivy did not see contraction of gall bladder of dogs after intraduodenal instillation of magnesium sulfate (10).

Injection of 50 cubic centimeters of 50 per cent sodium sulfate into the duodenum of 4 dogs (Figs. 2 and 3) produced a consistent spasm of the sphincter and the duodenum, more prolonged than the initial response with magnesium sulfate with a slow return to normal activity. Sodium and magnesium sulfate have been recommended as cholagogues (1, 11) but if our results can be applied to man, they would cast doubt upon the accepted mechanism of their action.

Twenty cubic centimeters of 5 per cent magnesium oxide injected into the duodenum of 5 dogs produced marked and prolonged increase in the resistance of the sphincter and in duodenal peristalsis. The rise in sphincteric resistance frequently was out of proportion to changes in duodenal tone (Fig. 2). The gall bladder showed no response.

Olive oil, 32 per cent cream, egg yolk and a mixture of egg yolk and cream when intro-

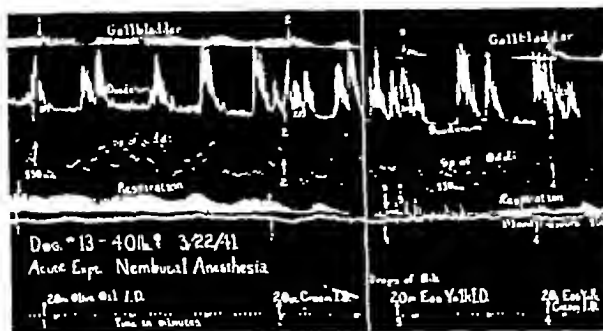


Fig. 4 At 1, the intraduodenal instillation of olive oil produced a contraction of the gall bladder and an initial coincident transitory spasm of the sphincter and duodenum, subsequently, the sphincter resistance fell to a level lower than what it was prior to injection. At 2, 32 per cent cream instilled into the duodenum, at 3, egg yolk, and at 4, a mixture of 32 per cent cream and egg yolk, had an almost identical effect, except that the latter two preparations produced more effective contractions of the gall bladder

duced into the duodenum produced similar effects—an immediate contraction of the gall bladder associated with a simultaneous increase in sphincter and duodenal tone of 3 to 4 minutes' duration (Fig. 4). Following this, sphincter tone falls to a level below that prior to injection for a similar interval and subsequently rises to its control level. We found a mixture of egg yolk and cream to produce the greatest contraction of the gall bladder of all agents injected into the duodenum. This response was not influenced by previous antispasmodic medication with atropine or traseptin (diphenylacetyldiethylaminoethanol hydrochloride).

In summary of our results with agents injected into the duodenum, acid substances such as gastric juice and 1/10 normal hydrochloric acid produced relatively short increases in resistance to bile flow. Relatively neutral media, such as magnesium sulfate and sodium sulfate, increased the tone of the sphincter out of proportion to their effects on the duodenum. Alkaline media such as sodium hydroxide and magnesium oxide, produced marked simultaneous responses in the sphincter and duodenum which would appear to oppose the flow of bile the longest. It is to be remembered that it is an increase in duodenal tone, and not so much of motility, that opposed the flow of bile. None of these agents introduced into the duodenum showed a con-

sistently uniform effect on the gall bladder. The latter may have been due to the washing-out effect of the constant perfusion with 0.9 per cent sodium chloride solution, by which substances like cholecystokinin may have been eliminated. This is not probable, however, because a number of tests were carried out in the beginning of experiments when little washing-out could have occurred.

ANALYSIS OF STUDY

The entrance of gastric juice or rather of the hydrochloric acid of the gastric juice, has been held responsible chiefly for the liberation of cholecystokinin in the duodenum and jejunum. Therefore small quantities of gastric juice or dilute hydrochloric acid were perfused through the duodenum. Contraction and rise of tone occurred simultaneously in both sphincter and duodenum, but the gall bladder was hardly affected in most experiments. We know from experience with pancreatic secretion following introduction of hydrochloric acid into the duodenum that the secretin mechanism may be fatigued. It is possible, therefore, that the absence of gall-bladder contraction following injection of gastric juice into the duodenum may be explained on a similar basis, namely that the constant perfusion of the duodenal segment by the saline solution may have washed out preformed cholecystokinin. This is questionable, how-

ever because in the numerous experiments performed a number were done after a short perfusion only of the duodenum and yet with the same negative results on the gall bladder. Furthermore various fats were effective when introduced in a like manner.

If gastric juice or hydrochloric acid produce spasm of the sphincter and duodenum this may explain why bicarbonate or other antacids are beneficial in certain cases of disease of gall bladder and extrahepatic system. The effects of gastric juice and of hydrochloric acid were unaffected by small intravenous doses of atropine or trerentin.

The effect of alkaline solutions administered intraduodenally deserves discussion because some of the alkalies taken by mouth will appear in the duodenum as sodium hydroxide, and because magnesium oxide is used largely in the treatment of upper abdominal distress. Figures 2 and 3 illustrate that administration of magnesium oxide and sodium hydroxide was followed by marked subtetanic contraction of duodenum and sphincter the latter being more prolonged than the former (Fig. 3). Although the degree of dilution in the stomach and gastric emptying time in the human after ingestion of alkalies may modify such a response considerably the above observations should be kept in mind.

The ability of egg yolk and cream to act as gall-bladder evacuants has been amply described by Boyden, but its effect on the sphincter has not been emphasized. The initial phase of spastic contraction of sphincter and duodenum might well account for the "two minute pause" described by Boyden (4) as elapsing between the entrance of this material into the duodenum and the evacuation of the gall bladder.

SUMMARY

1. The introduction of various agents into the duodenum was associated with immediate spasms of the sphincter of Oddi and of the duodenum of varying duration the more alkaline media (such as sodium hydroxide and

magnesium oxide) appearing to oppose the flow of bile the longest.

2. Magnesium or sodium sulfate had a variable effect on the sphincter of Oddi and duodenum of the dog with no consistent effect on the gall bladder.

3. Fats introduced into the duodenum effectively contract the gall bladder the most effective preparation was a mixture of egg yolk and cream.

4. The initial spasm of the sphincter of Oddi and duodenum produced by intraduodenal instillation of fats is suggested as a possible explanation of the "two-minute pause" described by Boyden as the initial phase in the evacuation of the gall bladder.

5. The independent activity of the sphincter and duodenum during various phases of the response to magnesium sulfate is offered as further evidence that they are independent physiological mechanisms, although frequent ly similar in their reaction.

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A NEW METHOD OF REPAIR FOR INDIRECT INGUINAL HERNIA CONSIDERED IN REFERENCE TO PARIETAL ANATOMY

W KENNETH JENNINGS, M D , F A C S , BARRY J ANSON, Ph D (Med Sc), and
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THE problem of repairing inguinal hernia remains unsolved despite the memorable contributions of Bassini and Halsted. The numerous modifications of the operation introduced by those pioneer surgeons, indicate that, although both methods have shown the way to far better results than were obtained earlier, neither has proved to be a completely satisfactory solution. Prior to the introduction of these techniques, recurrences were so common that most physicians despaired of curing the condition, one reads of recurrence rates in a single series reaching as high as 90 per cent. It is little wonder, then, that a method which enabled surgeons to reduce this high incidence of failures to a figure around 10 per cent should be widely adopted and accepted by most as a satisfactory operation.

A survey of the literature convinces one of the lack of agreement among authorities as to the frequency of recurrence with present day surgical methods. This may be attributed to a number of factors, chief among which is the difficulty of accurate follow-up examinations over a sufficient period of time in any large series of cases. Zimmerman warns against the fallacy of accepting verbal or written communications from patients as reliable information, he maintains that only by careful examinations, covering a period of several years, is the surgeon justified in drawing conclusions as to results. Few series of cases have been reported in which such re-examinations have been carried out for more than 75 per cent of the patients in the series. Moreover, it is probable that the rate of recurrence is much higher among the cases not followed, for many of those who suffer a return of the original trou-

ble are quite likely to go elsewhere for further advice and treatment. Most hernia sufferers have a friend who has experienced a recurrence following an attempted surgical repair and all have been warned concerning this danger, it is only natural that many of those who suffer a recurrence should abandon hope of securing permanent relief through surgery, and consult the truss-maker for further help. Aversion to the truss is the factor usually responsible for the return of the patient to the doctor—probably a new doctor. Of the last 4 cases of recurrent inguinal hernia in which patients were operated upon by one of the authors (WKJ) 3 had been patients of other surgeons who knew nothing of the secondary rupture. Although it is well known that a careful repair is seldom followed by recurrence under 6 months, the majority of statistical reports include patients recently operated upon as well as cases which have been observed for longer periods. Inasmuch as most surgeons today employ the Bassini technique, or one of its numerous modifications, it is difficult to reconcile the widely divergent results reported by men whose experience in this field should establish them as authorities. It would seem, therefore, that the higher figures for recurrence are most reliable (Table I). This contention is further substantiated by the abundant literature on the subject, as well as by the numerous operative procedures recommended for its correction.

A new principle in the treatment of femoral hernia was recently proposed by Professor Henry, of Cairo, Egypt, who described a procedure in which the femoral ring was exposed by a retroperitoneal approach through a low midline incision. The advantages which such an operation provide are (1) direct exposure of the opening through which the hernial sac

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TABLE I.—INCIDENCE OF RECURRENCE REPORTED WITH USUAL OPERATIONS FOR HERNIA

Author	Cases	Followed	Indirect per cent	Direct per cent	Recurrence per cent	Total per cent	Remarks
Albarr	314					66	Examination
Adair	100	773				97	Examination
Andrews and Russell	48			37			Examination
Bark	484					80	Quadrantotomy
Boman	113	773					Quadrantotomy
Burkefeldt	146	773					Examination
Black	20,709 2044	Collective statistics				3-5.5	Total series Examination
Cattaneo	20,000					—	No follow up
Dresser	200						Follow up?
Faust	500 200	2-100 773 77 of 2000				8	Examination Examination
Glenn and McBride	200	6-24 2000	37		30		Examination
Grace and Johnson	24	2-10 773			34		Patients all over 20 yrs old
Guth	62	2-1 773					Quadrantotomy
Hansen	1,300					8	No follow up
Jones	30	77					Examination
Lohmann	200	—10 773					Examination
Mason and Potts	20	2-17 2000				6.8	Examination
Osfield	230	773 up		20			/ returned
Pugh	200	2-9 773	20	23			Examination
Parsons	111 470	Calicut R.R. } 77 200 40	8 10	6 20			Examination Examination
Schaefer	1,000	1-10 5 773			6		Examination
Spangue	204						Examination
Stanton	207	2-10 773					Follow up?
Wachsmuth and Reber	107					1	Examination

*Zimmerman, L. M. Internal Abstract Surg. 229, 26

protrudes, (2) guarantee of high ligation of the sac, and (3) avoidance of scar tissue in the inguinal sector of the abdominal wall. In the carrying out of this procedure it was observed that excellent exposure of the abdominal inguinal hiatus was possible by a slight additional retraction of the rectus muscle laterally. This observation suggested that a procedure, similar to the one proposed by Henry but adapted to the requirements of indirect inguinal hernia, might possess fundamentally the same advantages.

The standard accounts, to which the anatomist and surgeon have accustomed themselves, describe the inguinal canal as an indefinite "space" of oblique course whose parietal constituents are strong representations of the layers which make up the abdominal wall. In

these accounts the subcutaneous orifice of the canal is loosely termed a "ring" and the degree to which muscle fascicles of the internal oblique are drawn outward through this orifice is often exaggerated the fascial contribution from the transversus abdominis is inadequately described and the adipose continuation of the preperitoneal connective tissue is usually disregarded. In almost every instance inguinal anatomy is presented as if it always conformed to a definite pattern. In view of these facts, it was considered desirable to re-examine the inguinal strata carefully—and by dissection, in the order in which they would be encountered by a hernia. This posterior approach proved to be particularly applicable to the surgical method presented since the latter technique affects primarily the deeper abdominal layers

I ANATOMY

Serial dissections were carried out in an unusually favorable, muscular, white male,¹ and an accurate drawing was prepared of each of the several stages in the dissection. In the descriptions of the important anatomical features thus recorded, the innermost stratum will be considered first, the external oblique last, since this is the succession in which a hernial mass encounters the series of parietal laminae.

a Peritoneum The peritoneum of the left side of the specimen illustrated is of the normal adult disposition, elevated in low folds over the middle and the lateral umbilical ligaments (Fig 1).² On the right side, in addition to being draped over subperitoneal ligaments, the peritoneum is carried outward as a serous hernial sac which is the persistent processus vaginalis (Fig 1). Through the serous layer are visible the linea semicircularis, rectus muscle, inferior epigastric vessels and the line of the inguinal ligament—the muscle, artery, and ligament bounding the triangular space (of Hesselbach) to the lateral aspect of which the hernia protrudes.

b Preperitoneal tissue Through much of the inguinal area the layer of preperitoneal connective tissue is of cobweb-like texture, almost devoid of fat (Fig 1, left half). Within it are imbedded the several umbilical ligaments, and the inferior epigastric vessels. The

preperitoneal layer, along the pelvic wall, is considerable in amount, traced outward from the abdominal inguinal “ring” it is lost in the proximal part of the inguinal canal. In many specimens, however, this funicular continuation of the retroperitoneal tissue is appreciable in amount, forming a lobulate collection deep to the internal spermatic fascia, in bulk it may then equal the combined mass of the other constituents of the cord. It would, assumedly, constitute a resilient tissue easily compressible under pressure of an advancing indirect inguinal hernia.

c Transversus abdominis muscle The transversus abdominis muscle is almost universally described as forming a superior boundary for the inguinal canal, its fascia a posterior wall, the fascial layer which is invariably described is the internal investing, or transversalis, fascia, the thinner external layer is disregarded.

In the specimen herein illustrated, the transversus abdominis, as usual, becomes aponeurotic and fascial as the inguinal canal is approached (Figs 2 and 3, cf Fig 5, McVay and Anson, 1940), the lower part of the transversus (i.e., the area at the inguinofemoral border) is totally fascial, no aponeurotic fibers being seen in the part prolonged upon the cord. The layer is so thin that the yellow fat preperitoneal is plainly visible through it, in spite of the fascial character, it is removable, as a whole layer, from the fat.

In the standard accounts the transversalis fascia—which is the internal one of the two investing fascial layers of the transversus—is treated as if it were the sole contributor to the internal spermatic fascia. Yet the thinner external layer of investing fascia contributes part of the substance of the latter, although to lesser degree, the external investing layer is traditionally disregarded, assumedly because, in the course of regular dissection, it is removed to expose the muscular portion of the transversus.

In the current specimen the transversalis fascia is a strong and definite layer on the inner aspect of the transversus abdominis. On the right side, carried into the inguinal canal, it forms a fascial diverticulum situated just lateral to the inferior epigastric vessels (Fig 2, right half), this is, of course, the tubular pro-

¹The specimens are adult white cadavers of a average height and weight.
²In addition to the descriptions presented in the legends, the following comments on the dissections may be of interest to the reader. In Figure 1, for service in topography, the pelvic and perineal structures are included in the drawing: in the pelvis, urinary bladder, prostate (hypertrophic), sectioned in the plane of the prostatic urethra; pelvic diaphragm, obturator internus muscle, alae ischiopubic rami, acetabula, etc. in the perineum, urogenital diaphragm (superior to which the dorsal veins of the penis enter the pelvis), erectile bodies (with muscles) at the level of the bulb of the urethra. The most inferiorly placed layer is the fascia of Colles (deep layer of the perineal superficial fascia). Structures situated external to the pelvis have been removed. The outline of the margin of the rectus sheath, the boundaries of Hesselbach's triangle are seen. In Figure 2 the urinary bladder has been drawn backward to expose the pubic part of the bony pelvis, the obturator vessels and the pubic branches of the obturator arteries. The pelvic diaphragm is included in the area illustrated but not the structures inferior thereto. In Figure 3 the bladder and prostate (with large plexiform veins) have been excised to show the important bony structures in the anterior part of the pelvis. Further, in removal of the obturator and superior diaphragmatic fasciae, the pubic portions of the levator ani and obturator internus have been exposed on both sides, the pubic symphysis, inferior pubic rami and pubic arcuate ligament are shown, also the dorsal penile vein in relation to the arcuate ligament and the transverse pelvic ligament. The bulb of the urethra (marking the level of the superficial perineal compartment) remains as an additional landmark. Vessels have been removed except for the following: distal parts of the external iliac arteries and veins, upper reaches of the inferior epigastric arteries with branches laterally to the muscles of the inguinal wall, dorsal vein of the penis (at the pubic arcuate ligament), the arterial plexus (left side) from the pubic branch of the obturator artery. In Figure 5 the urogenital and pelvic structures are also removed, in order to demonstrate fundamental bony relations: symphysis and rami (superior and inferior) now freed of muscular and aponeurotic attachments.

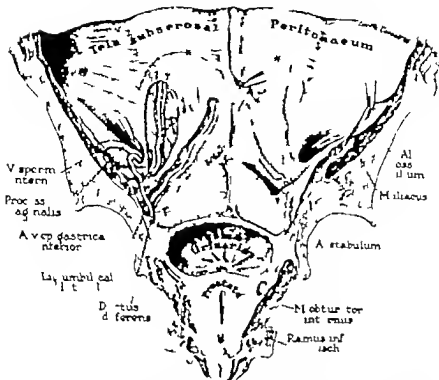


Fig. Internal aspect of the anterior abdominal wall. Peritoneum and preperitoneal connective tissue (see also footnote). The pelvis has been coronally sectioned, the line of section passing through the iliac fossae, acetabula, and ischial ramus. On the right (normal) side the peritoneum is intact; on the left (normal) side it has been removed to expose the preperitoneal layer in which lie the umbilical ligaments. The preperitoneal layer has been removed only along the course of the inferior epigastric artery. Through it (right side) are visible rectus muscle, inferior epigastric artery, linea semicircularis. The iliac fascia of the greater pelvis has been freed from muscle as has, likewise, the thin preperitoneal layer from the muscle fascia. The peritoneum remains on the right half of the superior surface of the urinary bladder; on the left the combined preperitoneal and endopelvic fascial layers are exposed.

elongation of internal spermatic fascia dilated by hernial protrusion. Medially it is carried upward in the midline as a thickened, pointed process, the adminiculum. Where the transversalis fascia reaches the lateral margin of the rectus muscle it splits to form the rectus fascia (Fig. 3). It is easily dissectable from the muscle in the area below the semicircular line; however, it cannot be easily separated as a distinct layer from the aponeurosis of the transversus either along the lateral border of the rectus abdominis or upon the latter muscle itself above the level of the semicircular line.

d. Internal oblique muscle. The lower inguinal part of the internal oblique—with the subjacent and corresponding portion of the

transversus abdominis—arises from the iliopectineous fascial tube, not from the inguinal ligament (McVay and Anson, 1940, Figs. 1 and 3). The attachment to the inguinal ligament is accomplished only through the fasciae which cover the opposed surfaces of the muscle and ligament. The muscle fibers usually descend, closely grouped on the posterolateral aspect of the spermatic cord. It is exceptional to find more than a fascial remnant of this stratum ascending on the medial side of the cord to a public insertion.

The statement (in italics) that the superficial muscle layer of the external oblique and internal oblique are continuous with the linea semicircularis, etc., is entirely erroneous, as is derived from the aponeurosis. When the general layer of external covering fascia (the lamina propria) is removed, the fibers are merely local aponeuroses, the fascial layer prolonged, the fibers appearing to be directed just behind to the part of the fascia which is displaced, the fibers are not aponeurotic.

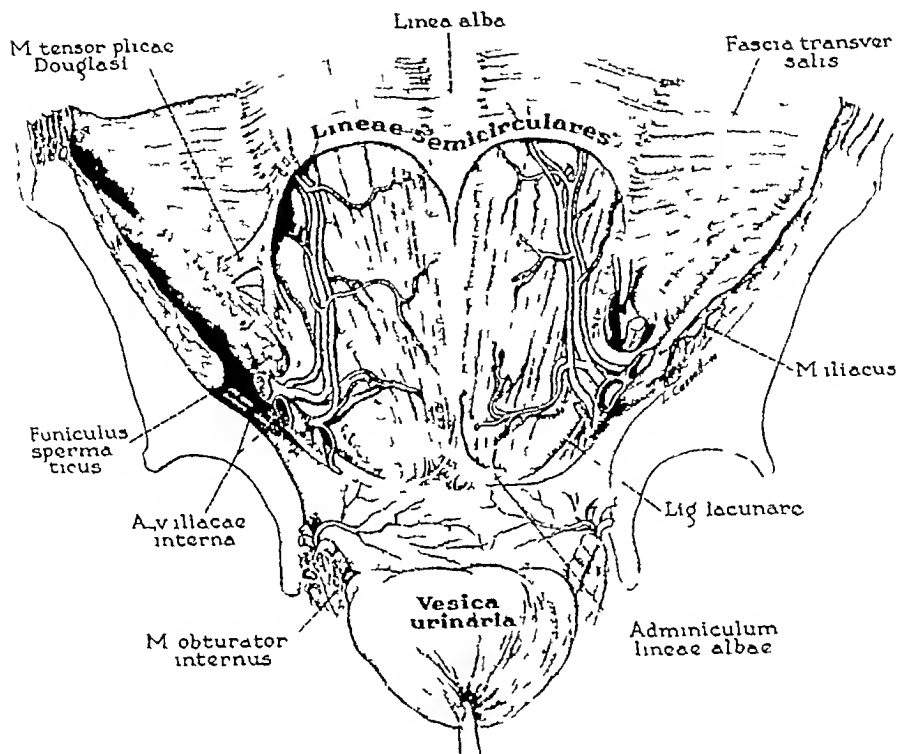


Fig. 2 Abdominal wall from within transversalis fascia. The preperitoneal tissue has been removed, the transversalis fascia and iliopsoas fascia exposed.

On the right side the layer is displaced from its natural site, lengthened to invest the protrusion (Fig. 4), as if incapable of excessive prolongation, the muscular fascicles are carried but a fraction of the way, the more resilient fascia through the full extent of the testicular descent. Just as the investing fascial layers of the external aponeurosis are protruded between crura, so the comparable layers of the internal muscle are stretched between adjacent muscle fascicles. The cremasteric fascia is, then, a definite sheet, not merely an areolar filling—so definite that, although muscle fibers are commonly sparse in the cremasteric fascia, it remains as a layer so readily separable that it is demonstrated in virtually all student dissections.

c External oblique muscle. It should now be clear that in a consideration of the three abdominal layers, a sharp distinction must be drawn between the musculo-aponeurotic and

the fascial elements, failure to do so accounts for the ambiguity of some current descriptions and for the incorrectness of others. Although muscular fascicles and aponeurotic bands may terminate rather abruptly to form free margins, the associated fascial layers continue uninterrupted to bone, aponeurosis, or other fascia, when drawn away from its original site, each stratum maintains its continuity with the undisplaced portion of the same layer. Because these simple concepts are not carefully regarded, the true nature of the subcutaneous inguinal ring is not made clear in some textbook descriptions.

The interval in the aponeurosis is triangular in outline, any annular character is due to the presence of fascial tissue. The cleft, in the authors' experience, is elongate, not uncommonly extending superolaterally as far as the muscle belly or even to the anterior superior iliac spine.

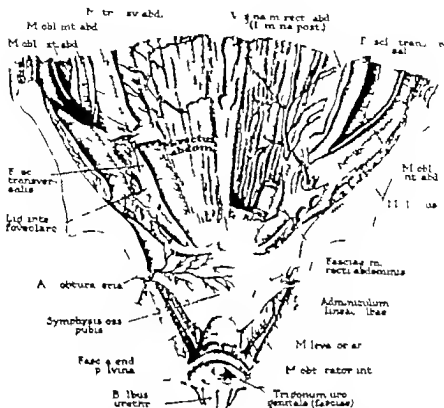


Fig. 3. Abdominal wall, continued: transverse abdominis muscle and aponeurosis, and the layers' contribution to the spermatic cord. The transversalis fascia has been removed from both sides. On the right side additionally the transversus abdominis muscle has been cut away in a V-shaped area, exposing the internal oblique. At the lateral border of the right rectus abdominis muscle, a window has been cut to expose the layer of rectus fascia (derived from the trans crura), which passes in front of the muscle. The aponeurosis of the transversus (medially) is intact, and is distinguishable from the layers of rectus fascia. The transversus has been circularly cut on the left side, additionally the internal oblique is cut away in a V-shaped piece near the anterior superior spine, showing the muscular part of the external oblique, and the investing fascial layers on the abdominal aspect of each of the muscles. The adipous muscles have been removed from the iliac fossae except near the inguinal ligament. The transected external iliac vessels rest upon the iliopectineus of each side.

The superior crural and the neighboring fibers spread out evenly upon a flat surface of pubic attachment: there is no evidence of marginal thickening or of local clumping; the front of the pubis, inferior to the level of the crest, is wholly covered by aponeurosis (Fig. 1, Anson and Ashley, 1931). All descriptions emphasize the concept of crural boundary of a triangular intercolumnar space; but when the superior crus is cut and turned aside, the attachments of the crura are shown to be surprisingly far apart, the external orifice broad

when the horizontal distance is considered (Fig. 2, Anson and Ashley, 1931). The superior crus attaches along a line on the front of the pubic body, several centimeters inferior to the level of the crest (when the oblique distance between crura is 1.0 cm; for example, the transverse may be as great as 3.0 cm). The orifice therefore extends almost to the symphysis. When levated by a herniating mass, the superior crus would be merely a constricting band on the anterosuperior aspect of triangular osseoponeurotic foramen.

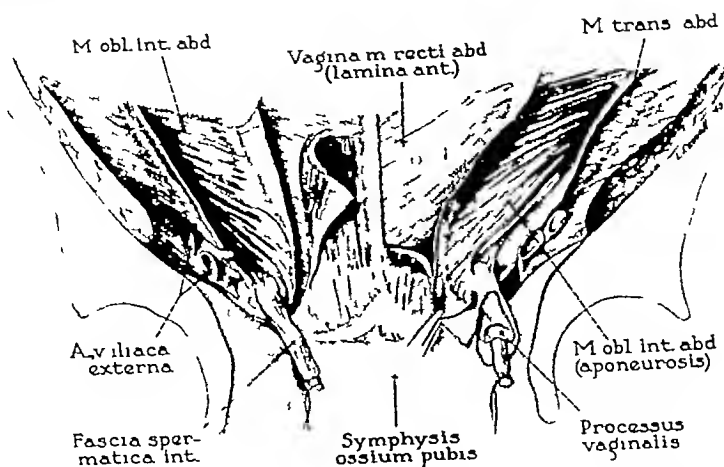


Fig 4. Abdominal wall, continued internal oblique layer On the right (hernial) side the transversalis fascia and transversus abdominis remain at the marginal attachments only, and upon the sac, the internal oblique, is, therefore, almost entirely exposed For purposes of comparison, on the left side the exposure is similar

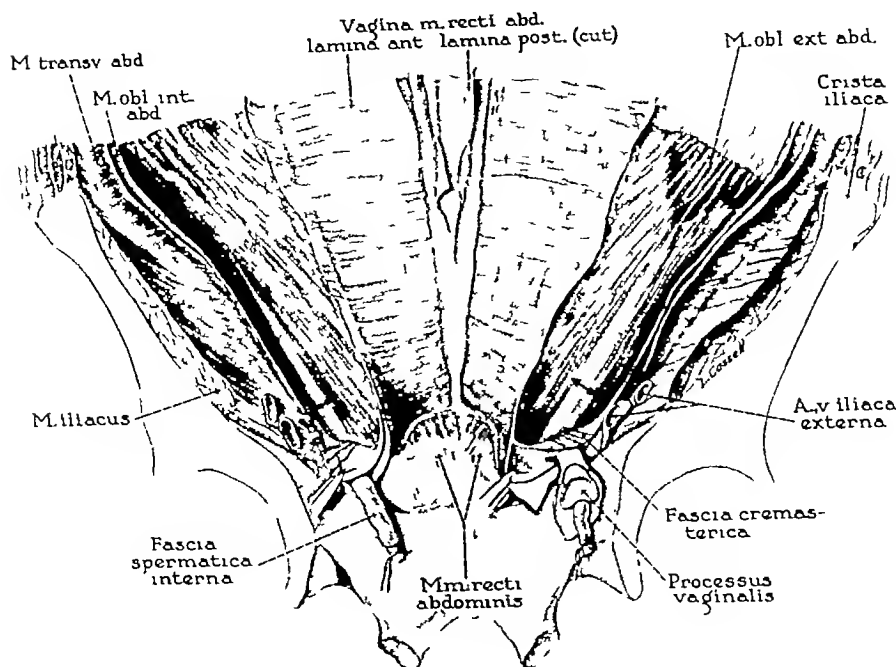


Fig 5 Abdominal wall from within, concluded external oblique muscle and aponeurosis (freed of internal investing fascia except in a small area on the right side) The internal oblique has been almost entirely removed, the rectus and pyramidalis muscles have been excised to show the anterior layer of the rectus sheath, the transversalis and rectus fascia have been removed except at the attachment along the pubic crest. The internal spermatic fascia is present as a constituent of the hernial sac The transversus abdominis muscle appears merely as a narrow strip along its inferior attachment The funicular part of the internal oblique is chiefly fascial The triangular cleft in the external oblique aponeurosis of each side is demonstrated (margins indicated by arrows), as is the thin fascial layer which crosses the space in the aponeurosis

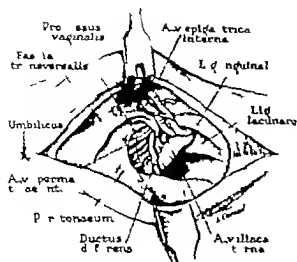


Fig. 6 Exposure, in an anatomical specimen, of the structures at the abdominal inguinal ring, through median incision (anastomosis to epiphysis) simulating that proposed, surgically, in the current article. The margins of the incision have been retracted, the peritoneum has been displaced by blunt dissection. By this procedure the ring is exposed retroperitoneally, also shown are the following structures which are associated with the abdominal ring: external iliac vessels as they near the femoral canal, the inguinal process of the peritoneum, the spermatic vessels and the ductus deferens as they run together to form the cord, the inferior epigastric vessels as they lie to the medial side of the abdominal inguinal ring.

The inherent weakness in the area of the "subcutaneous inguinal ring" is not due to a lack of intercrural fibers medially. Strong fibers of this type are not placed with such restricted and definite distribution, usually being lodged in the outer layer of investing fascia of the external oblique aponeurosis above and to the medial side of the aponeurotic cleft (McVay and Anson 1940). It is the general fascia, not these special fibers which forms the funicular covering. The intercrural fibers are quite subsidiary and are not carried downward on the cord.

The fascia at the aponeurotic hiatus is not merely external investing (innominate) fascia. It is bilaminar in origin, consisting of an internal investing layer as well as the two fused back-to-back. Thus fused as an intercrural or intercolumnar fascia, the single (conjoined) layer is prolonged upon the cord as the external spermatic fascia. As already stated the separately definable intercrural fibers do not extend in their distribution to the medial area of the aponeurotic cleft and, consequently, do not contribute to the substance of the funicular tube. In fact, the intercolumnar fascia is thin just near the site of prolongation. This means that there is regularly an area of weakness between the aponeurotic crura, in herniating the mass merely separates further the crural boundaries of a triangular area whose covering tissue

is fascial only (Fig. 5).¹ Having widened the thin funicular "sac" formed by external spermatic fascia, the hernial mass pushes outward through the intercrural space. The strong crura then tend to return to normal position, with the result that the external fascial sac, the contained saccular coverings derived from the successively deeper abdominal strata, and the true hernial contents, are clamped between columnar (crural) "ligaments" (see Figs. 1 and 2; Ashley and Anson 1941). Therefore not only does the fascial part of the external oblique constitute an inefficient barrier against hernial protrusion but the marginal aponeurotic bands are readily displaced to permit of egress.

II. SURGERY

These anatomic studies afforded a better understanding of the structural relations as encountered in a retroperitoneal approach to the inguinal canal and convinced us that in principle any operation which effects a high ligation and removal of the hernial sac, closure of the so-called abdominal inguinal ring and avoidance of any trauma to the transversalis fascia, or other structures about the inguinal canal is fundamentally sound. Accordingly a technique was planned in which the low mid-

¹It should be noted on a matter of record that the inguinal sac is not a true sac, but a "transversalis" capsule, above the femoral vessels and below the inguinal ligament. The transversalis arises from the superior iliac crest and runs in a horizontal line to the lesser pelvis. In addition, the inguinal sac is not a true sac, but a "transversalis" capsule, above the femoral vessels and below the inguinal ligament.

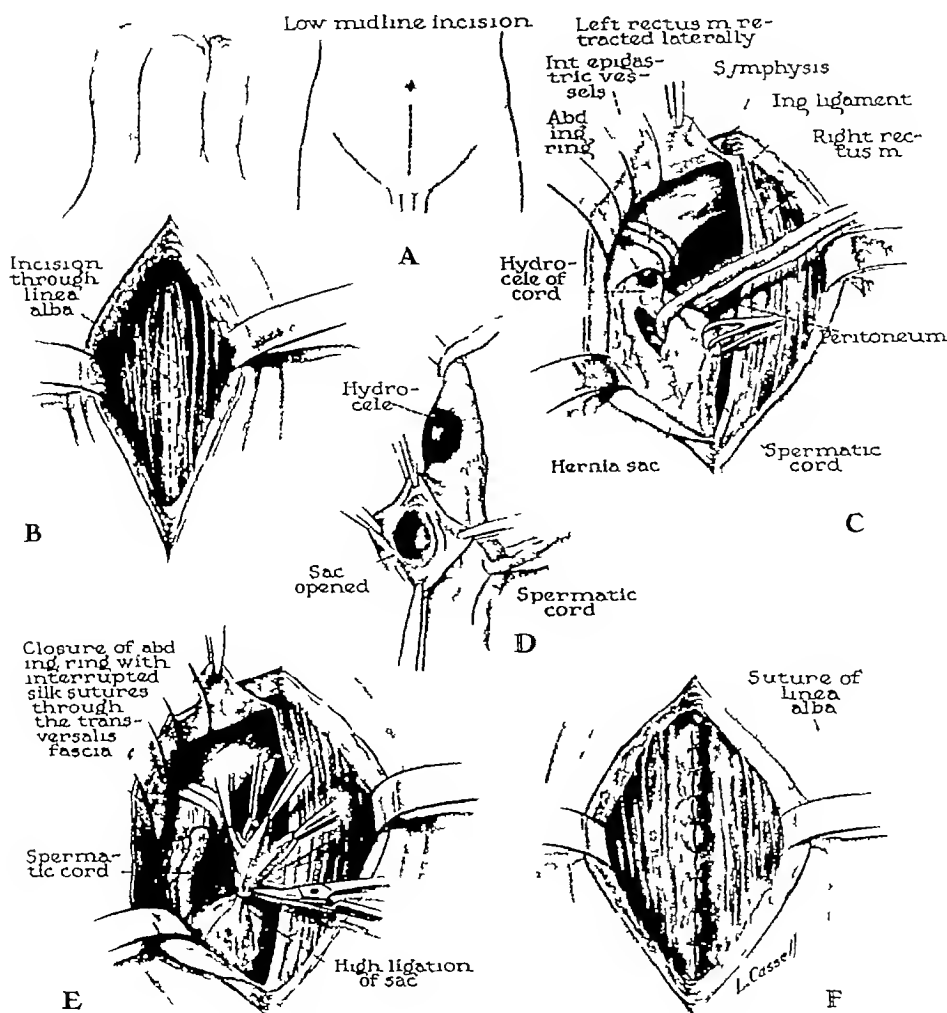


Fig 7 Technique for the repair of indirect inguinal hernia through low midline incision A, Skin incision, B, incision through the fascia adjoining recti muscles, C, Separation of the left rectus muscle from the peritoneum by blunt dissection—the muscle is retracted laterally to expose the inguinal ligament, the structures of the spermatic cord and the abdominal inguinal hiatus A tape encircles the cord to aid in identifying and separating the hernia sac (small hydrocele of the cord is present) D, The sac, having been dissected free from the spermatic cord, is now opened, E, high ligation of the sac is completed and the sac is excised, 2 interrupted silk sutures have approximated the transversalis fascia in order to reduce the size of the abdominal inguinal ring (the lower leaf of transversalis fascia is obscured by adipose tissue), F, The fascia is closed with interrupted silk sutures

line incision described by Henry is used (Fig 7, a), this is carried down through the rectus fascia at the linea alba (Fig 7, b) to the peritoneum, the latter being separated from the posterior surface of the rectus muscle by blunt dissection The urinary bladder may appear

in the lower field, in which case it is carefully pushed away from the overlying structures The lateral dissection is easily accomplished because of the loose areolar tissue between the peritoneum and the rectus muscle which separates readily The dissection is carried as far

TABLE II—INDIRECT INGUINAL HERNIA OPERATED UPON BY MIDLINE RETROPERITONEAL APPROACH

Patient	Age	Date of operation	Followed	Recurrence	Remarks
H	47	17-20			
C H		16-20	yr		Scrotal hernia
I P		20			Large hernia. Developed linear peritonitis third postoperative day
I P	13	20	yr		Large hernia
R M	26	17-20	10 mos		
G G		1-2-20	mos		
C B		1-2-21	mos		
G S		41	mos		Several hernias, large rings
S P		41	mos		
A D		2-6-21	mos		
M S		24-21	3 wk		Scrotal hernia

as the inguinal ligament in order to expose adequately the abdominal inguinal opening. With good relaxation of the abdominal muscles the rectus muscle now can be retracted laterally, thus exposing the "ring," which is identified by locating the inferior epigastric vessels (Fig. 7 c cf. Fig. 6). It is seen to lie across the inguinal ligament from the femoral ring in relationship to which it lies slightly anterior and lateral. The hernial sac is easily recognized as it enters the inguinal canal. Occasionally it is necessary to ligate and divide the epigastric vessels which may lie across the inferior margin of the ring. In order to facilitate mobilization of the sac. Gentle traction on the sac at the level of its junction with the peritoneum, together with combined blunt and sharp dissection, results in its easy separation from the other cord structures in the canal (Fig. 7 d). A sac which descends into the scrotum or one associated with dense adhesions may offer difficulty. In such instances it may be necessary to section and leave a portion of the sac. After removal of the sac (Fig. 7 e) the abdominal inguinal hiatus is closed with two or three interrupted silk sutures which merely approximate the transversalis fascia across the opening (Fig. 7 e). It is felt that unless the aperture is so large that it comes to underlie the subcutaneous inguinal opening, thus producing in effect a direct hernia, the obliquity of the angle by which any secondary

peritoneal protrusion would have to enter the newly closed abdominal ring together with the strength of the intact wall are sufficient to insure against any danger of recurrence. The operation is concluded by the suture of the fascia in the midline (Fig. 7 f) and the approximation of the incised skin margins with interrupted silk sutures or Michel clips.

The advantages of such a procedure are several. Protection is offered against recurrence afforded by the avoidance of distortion trauma and the formation of scar tissue in the vulnerable inguinal area. The technique itself is much simpler than that employed in the orthodox methods for repairing an indirect inguinal hernia. The procedure can be carried out more rapidly. There is little danger of injury to the ilioinguinal nerve and to the structures of the spermatic cord finally there is less likelihood of wound infection than with an inguinal incision.

It should be pointed out, however, that the operation has certain limitations. Obviously such a method of repair is unsatisfactory for a direct inguinal hernia and for a large indirect hernia in which the orifices of the canal have become so dilated as to create a window in the inguinal wall. The latter should be recognized and repaired in the same manner as a direct hernia. Good relaxation of the abdominal wall is essential to adequate exposure when the midline approach is used, hence the use of general anesthesia is excluded. Novocain infiltration anesthesia offers greater difficulty than it does with the inguinal approach because of the necessity of infiltrating a much wider area. The danger of entering the peritoneal cavity might be considered an objection to any retroperitoneal approach. However we are of the opinion that such an accident is not of serious importance in only one of our cases was the peritoneum opened and this was repaired at once with no subsequent disadvantage to the patient.

We have operated upon 11 patients during the past 2 years using the technique described. It is appreciated that such a small series of cases, only 5 of which have been followed for a year, can hardly be entered as proof of this method's superiority over other procedures. However a number of interesting observations have been made in following this group

which deserve recognition (Table II) An elderly obese male (Case 3, D P), was operated upon 14 months ago under spinal anesthesia for a large right indirect hernia, on the third postoperative day he developed type VII bilateral lobar pneumonia, there followed 2 weeks of violent coughing without damage to the repair and when he was last examined, 13 months after operation, there was no evidence of recurrence Another patient (Case 2, C H) was operated upon for a scrotal hernia, and it was necessary to leave the scrotal portion of the sac because of dense adhesions, when last examined 12 months later there was no evidence of hernia or hydrocele although this patient has been at his regular work (manual labor) since the second postoperative month The youngest patient in the series was 4 years of age, the oldest, 62 All cases have been accepted without regard to the size of the inguinal "rings," although it is felt that the procedure should not be used in cases in which these apertures have been dilated to a condition which constitutes a direct opening in the abdominal wall There have been no recurrences in any of the cases followed for a period beyond 3 months (2 patients recently operated upon have not been re-examined)

CONCLUSIONS

A re-study of the anatomy of the inguinal canal by means of dissections which begin with the abdominal inguinal hiatus and proceed through the successively deeper layers, indicates the accessibility of a hernial sac from a retroperitoneal approach and serves to re-emphasize the importance of the peritoneum and transversus abdominis layer and the transversalis fascia in determining the strength of the abdominal wall about the inguinal canal In the specimen illustrated — and in many others examined during the progress of laboratory study — the inferior part of each of the abdominal layers is found to be an almost totally fascial area, aponeurotic fibers and muscle fascicles are sparse in the lower inguinal territory The transversus abdominis and the internal oblique are there quite uniformly thin,

while the external oblique is locally weak at the intercrural hiatus in its aponeurosis, these strata, with the preperitoneal and peritoneal layers, all are to a degree attenuated where, in the form of funicular investments, they are prolonged from inguinal to scrotal level as a set of concentrically lamellated sacculations When, in a case of indirect inguinal hernia, the innermost or peritoneal, sac is occupied by herniating intestine or omentum, the other saccular extensions share in its dilatation, as a consequence the wall of each sac is stretched, the abdominal orifice of each is dilated and displaced

In the restoration of an adequate parietal barricade to hernia the serous sac is, of course, the fundamental anatomical element, its space is the only true inguinal "canal" Since its congenital presence offered the initial route for hernial progress, its obliteration logically constitutes the primary step in surgery of repair Furthermore, in carrying out the ligation of the peritoneal sac, that method would seem most rational which brings minimal distortion and stretching to overlying parietal layers which have already been inordinately stretched

A method of repair for indirect inguinal hernia which is designed to preserve intact the transversalis fascia and other structures about the inguinal canal, and which simplifies high ligation of the sac, is described To date 11 patients have been operated upon, and of these 6 have been followed for a period longer than 6 months with no evidence of recurrence We believe that the operation is anatomically sound, and we are confident that it provides certain definite advantages over the conventional methods

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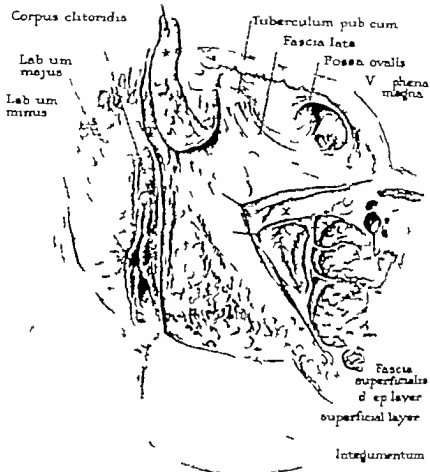


Fig. 1. Female perineum. Subcutaneous layers, specimen 1. On the (observer's) right side the superficial layer of the superficial fascia has been removed to expose the deep (Colles') layer in the anterior (urogenital) part of the perineum; in the posterior (anal) part of the perineum the superficial layer locally thickened and adipose remains intact behind the line of cut. In the rectoanal fossa the sleeve of fascia lata, shown by transecting the thick, has been freed from the muscle fascia, the latter is shown as it invests the anastomosis (at) and the adductors, freed from the muscles and retracted. The d. articular process has been mobilized and lifted (marked with star). On the opposite half of the perineum the skin remains intact. Successive deeper dissections of the same specimen follow (Figs. 2 to 4).

Further Studies: *Gynecological Anatomy and Related Clinical Problems*—Arthur H. Corbin, Barry J. A. Smith and Franklin L. Ashley.

FURTHER STUDIES IN GYNECOLOGICAL ANATOMY AND RELATED CLINICAL PROBLEMS

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IN continuing a re-study of the female pelvis and perineum in relation to the modern practice of surgery, additional anatomical features of gynecological importance have been established. Since many of these features are quite evidently not known to anatomists or surgeons because of dependence upon stereotyped accounts, the authors believe that a record of their experiences should prove serviceable.

In this third contribution concerned with a further study of the female pelvis and perineum, fifteen life-sized drawings were prepared by Tom Jones from three specimens.¹ Each drawing is an exact portrayal of the anatomy of a particular phase of the dissection, and none is a composite picture.

I PERINEUM SUPERFICIAL LAYERS

The superficial fascia of the perineum is fatty and is divided by heavy bands of fibrous tissue into lobules. The bands, in attaching themselves to the deep membranous layer in the urogenital part of the perineum (Fig. 1), render it difficult to find a definite plane of cleavage.

The fatty layer is relatively thin in the anterior part of the urogenital subdivision of the perineum,

but it increases in bulk as the base of the urogenital diaphragm is approached (Figs. 1 to 4). The greater lips are mound-like (Fig. 1), the elevation on each side being due in large measure to the presence of a fatty diverticular extension, into the labial tissue, of the inguinal superficial fascia (Figs. 2 and 3).

The prolongation is tapered and bluntly pointed (Figs. 1 and 3). This fatty process lies against the deep layer of the superficial fascia, therefore, in palpating the deeper perineal structures, the bulb of the vestibule is not felt, it is masked by the presence of the more superficially placed fatty process,² which is definitely demarcated from the surrounding tissue in which it is embedded, resembling a finger-like lipomatous tumor. Into it, for a short distance beyond the level of the subcutaneous inguinal ring, all the layers of the inguinal parietes are traceable as exceptionally thin investments (see Anson and Ashley, 1940). It contains the round ligament, which is, however, soon lost in the tissue which houses it.

The deep (membranous) layer of superficial perineal fascia is as distinct from the overlying fatty pannicle as the corresponding abdominal layer of Scarpa is from the layer of Camper (Figs. 1 and 2). The deep layer of superficial fascia is firmly attached at the sides along the ischiopubic rami, behind it fuses with the inferior fascial layer of the urogenital diaphragm, in front it is continuous, over the pubis, with the layer of Scarpa on the abdominal wall. The layer is complete, usually, save for the presence of small hiatuses—placed chiefly at the dorsal margin for the transmission of the clitoral branches and tributaries of the pudendal arteries and veins, posterior labial vessels sometimes pass through lesser hiatuses.

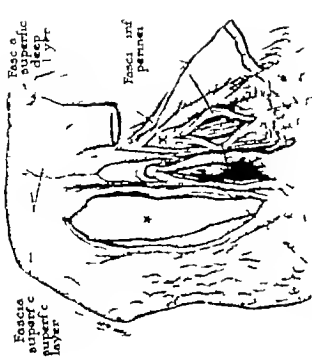
II PERINEUM SUPERFICIAL COMPARTMENT

On the next deeper level, within the superficial perineal compartment, lies the inferior perineal fascia (of Gallaudet), it is a thin, yet clearly

²The fatty process is 8.5 cm. long (measured from its root at the subcutaneous inguinal ring) it is 1.5 cm. wide at the midpoint. It extends posteriorly to a point opposite the hinder limit of the vestibule. Its failure to turn medialward in the area between the vestibule and the anal orifice accounts for the indistinctness of the posterior labial commissure.

¹A contribution from the Department of Obstetrics and Gynecology and the Department of Anatomy (contribution Anatomy No. 325) Northwestern University Medical School. Presented in part at the annual meeting of the South Atlantic Association of Obstetricians and Gynecologists, Richmond, Virginia, February 10, 1940, in part at the Annual Meeting of the Kentucky State Obstetrical Society, Louisville, Kentucky, September 30, 1941, in part at a meeting of the New York Obstetrical Society, New York City, November 11, 1941. Certain of the anatomical features were presented at the 1941 (Chicago) meetings of the American Association of Anatomists, April 9, 1941 (abstract Anat. Record vol. 79, no. 3, suppl. no. 4, pp. 4 and 5).

²As in previous contributions the accompanying illustrations are two thirds actual size. Specimen I (Figs. 1 to 4) was a white female, 30 years of age of average height, weighing about 90 pounds, embalmed. Specimens II (Fig. 5) and III (Figs. 6 to 15) were also white of approximately the same age et cetera. All were entirely free from gross pelvic or perineal pathology. In the current and in the preceding study (Curtis, Anson and Beaton, 1940) specimen III was employed for 10 and 7 illustrations, respectively. Figure 6 of the current set continues the dissection from Figure 7 of the earlier series. These two sets of illustrations constitute an atlas of musculofascial anatomy extending from the peritoneum on the pelvic aspect to the superficial perineal muscles on the perineal aspect of a single female specimen. It is the belief of the authors that such an inclusive treatment of an anatomical region in one specimen is unique. Specimen I was used in the detailed study of the superficial strata, specimen II for special dissection of the external anal sphincter.



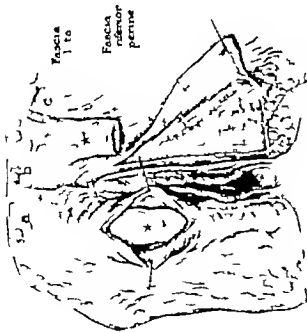
M. ischio-
convergens

M. bulbo-
convergens

Urethra

Vag. na.

Fig. 2



Fascia
superf.
deep
layer

superf.
layer

L. brum
majus

Fig. 1

(Legend: see opposite page)

separable, layer of deep fascia (Figs 2 and 3) Like a typical deep fascia (e g, of thigh, at λ , in Fig 1), it can be lifted away from the bulbocavernosus and ischiocavernosus as a thin sheet (Fig 3)

Internal to the inferior perineal fascia just described, immediately investing the bulbocavernosus muscle, there exists a much thicker layer which constitutes a rather loose sheath for the muscle (slit longitudinally to X in Fig 3) As determined by an examination of microscopic section, this sheath is chiefly fibrous, however, it contains scattered fascicles of skeletal muscle Apparently this ample sheath, not merely the muscle enveloped by it, is employed by Martius in his operation for relief of incontinence due to destruction of the urethra

The deep layer of the superficial fascia forms the floor of the superficial perineal compartment (Figs 1 and 2), into it are implanted fibers of the external anal sphincter (Fig 4, cf Fig 5) The roof of this compartment is the inferior fascia of the urogenital diaphragm (Fig 4, cf Fig 8) Since the two fascial layers (and the deeper elements as well) are attached directly to both sides of the pubic arch, they, with the external anal sphincter, form a sling-like support for the pelvic organs which is auxiliary to the pelvic diaphragm, the sling is narrow behind at the coccygeal attachment, broad in front of the ischial tuberosity (Figs 8 and 9) Within the superficial perineal compartment are contained the bodies of erectile tissue and superficial perineal muscles which are related to them, the muscles are, on each side, the

superficial transverse perineal, the bulbocavernosus and the ischiocavernosus (Figs 4 and 8)

1 *Superficial perineal muscles, vulvovaginal glands of Bartholin*¹ Within the superficial perineal compartment the crus of each side, although small, is definitely outlined, easily palpable against the ischiopubic ramus The bulb, on the contrary, is so flattened that its limits are not easily discovered

The bulbocavernosus muscles are situated on the sides of the vestibule (Fig 4, removed in Fig 8) As stated, a firm sheath of fibromuscular tissue encases the relatively thin inner layer of muscle, which, in turn, closely invests a bulbus vestibuli Posteriorly the muscle fibers of the opposite sides join behind the vaginal opening where they meet those of the superficial and deep transverse perineal muscles and the external anal sphincter Anteriorly, the bulbocavernosus divides, the medial division covering the so called intermediate mass of the erectile tissue, the lateral division covers the ischiocavernosus muscle (Fig 4) Contrary to accepted belief, it is the firm musculofascial sheath rather than the thin bulbocavernosus muscle which is of value in reconstruction operations on the female urethra, such as that employed by Martius The fibrous tissue of the bulb and the underlying firm tissues of the urogenital diaphragm offer additional surgical support (Figs 8 to 11)

The paired vulvovaginal (Bartholin) glands, outgrowths from the epithelium of the urogenital canal, are immediately adjacent and posterior to the bulbs, where they lie buried in cellular tissue, not definitely within the deep perineal compartment, as commonly described, but at the base of the compartment where the division between the

Fig 2 On the left, the superficial layer of the superficial fascia has now been exposed by reflection of the skin, it has been incised longitudinally where it covers the labial portion of the diverticular process (at star), the width of the latter demonstrated by retraction of the margins of the incision On the right, the deep layer of the superficial fascia has been cut, the flap turned lateralward, to show the inferior perineal fascia as the latter covers the muscles in the superficial perineal compartment. In the anterior portion of the anal part of the perineum, on each side, much of the fat of the superficial layer has been removed from the ischiorectal fossae, over the front of the pubis it has been removed in three levels to show, successively, the immediately subcutaneous tissue, *a*, the covering of the diverticulum, *b*, the diverticulum itself, at star, and the subjacent fascia lata, *c*

Fig 3 On the left side the fatty inguinal process (at star) has been further freed from the superficial layer of the superficial fascia by retraction of the margins of the now lengthened labial incision On the right the corresponding structure has been transected at pubic level, the membranous (deep) layer of the superficial fascia and the muscle fascia have been reflected Over the bulbocavernosus muscle the thick fibrous investment has been incised (to point marked X), the margins retracted Here five successive strata are demonstrated (skin to muscle)

¹Very frequently it is important to know the dimensions of structures in the perineal compartments equally important may be their relation to palpable landmarks Since such data are almost totally absent from standard descriptions and excessively rare in the literature It is thought worthwhile to furnish records of this kind especially where they are directly referable to accurate drawings made from the dissections illustrated

For specimen I (see esp Fig 4) the following measurements may be recorded The ischiocavernosus muscle is 10 cm long 1 cm wide at the midpoint The bulbocavernosus is 7.5 cm long the maximum width is 1.6 cm (mid bulbar) the thickness is 1.0 mm The vulvovaginal (Bartholin) gland is 0.8 cm long 0.35 cm wide From the medial extremity the duct is given off the latter is 1.25 cm long It empties into the vestibule 1.8 cm from the anterior midline 1.6 cm from the posterior (measured along an anteroposterior midline) The duct is 0.2 cm in diameter at the termination, 0.15 at the origin The superficial transverse perineal muscle (each) is 0.3 cm thick (at midpoint) 4.2 cm long (to midline from tuberosity) The external anal sphincter ani is 7.3 cm long (tip of coccyx to perineal body) 1 cm wide On the lateral wall of the ischiorectal fossa (the distance between the urogenital and the pelvic diaphragm is 3.5 cm (this is the height of the anterior recess of the fossa at the latter's posterolateral boundary) Along the same line the distance from the pelvic diaphragm to the surface of the skin is 6.5 cm — which is the depth incidentally of the mass of the fat filling the fossa It is 3.0 cm from the urogenital diaphragm (inferior fascia) to the skin In specimen III the superficial transverse perineal muscles together are 10.5 cm long which measurement is also that of the maximum width of the urogenital triangle Each muscle is 0.2 cm thick 0.3 cm deep and 0.7 cm wide The fibers of the ischiocavernosus muscle extend to a point 3 cm beyond (dorsalward) the attachment of the clitoridal crus

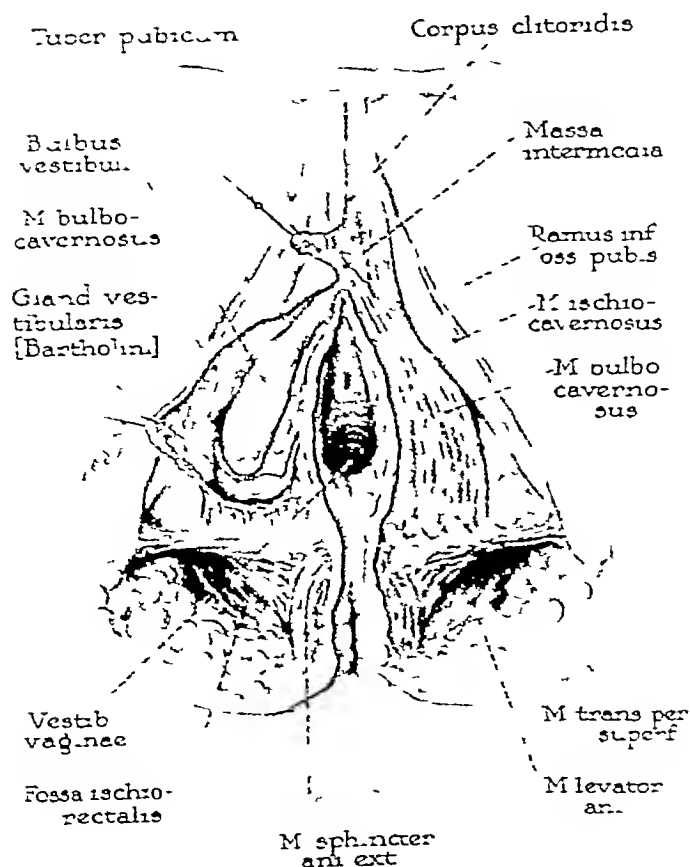


Fig 4. In the anal part of the perineum the levator ani and external anal sphincter muscles of each side are shown by removal of the superficial fatty tissue. In the urogenital part of the perineum on the right side by cutting away the muscle fascia, the ischiocavernosus, superficial transverse perineal, and bulbo cavernosus muscles have been brought into view. On the left side the bulbo cavernosus muscle has been reflected to expose the bulb of the vestibule and greater vestibular (Bartholin's) gland and duct. Anteriorly are seen the glans body, and intermediate mass of the clitoris.

laminae which invest the musculature of the urogenital diaphragm, the fasciae' (ofttimes as strong as aponeuroses), together with the muscle, make up the diaphragm.

The urogenital diaphragm is regularly described as triangular in outline; actually it is of quadrangular form. The pouch which its fascial layers forms does not completely segregate the contained muscles, since the deep and the superficial transverse perineal muscles blend medially (Fig 9). The musculature not only serves as a urethral sphincter (sphincter urethrae membranaceae) but extends superior to the coccygeal extension of the

external anal sphincter to a firm coccygeal insertion (Fig 10). In this respect it resembles the pubococcygeal part of the levator ani (Figs 6 and 7). When the urogenital diaphragm has been entirely separated from its posterior attachments, and reflected, the pelvic diaphragm still remains as a complete partition (Fig 12). Thus, the urogenital diaphragm does not fill a defect in the pelvic diaphragm but, rather, constitutes an additional re-enforcing layer for support of the pelvic organs.

In the specimen illustrated, a subdivision of the muscular components of the diaphragm into deep

transverse perineal muscle and urethral sphincter is not apparent (Fig. 9). The deep transverse perineal muscle of the urogenital diaphragm does not terminate sharply along a transverse line; a triangular prolongation passes backward, on either side of the rectum deep to the coccygeal extension of the sphincter ani (Fig. 9). The full extent of this prolongation of the urogenital diaphragm is revealed when the anal sphincter is removed (Fig. 10). The fascicles of the two sides converge, intermingle behind the anal canal and extend to a narrow coccygeal attachment, lying between the anal sphincter and the pelvic diaphragm, considering this hitherto undescribed element as an integral part of the urogenital diaphragm, the latter is, as previously stated, quadrangular not triangular. Many of the backward-directed fibers from the urogenital diaphragm penetrate the substance of the anal sphincter around its anterior three-fourths, interdigitating with these fibers and with the downward continuation of the levator ani (Figs. 10 and 11); other fibers continue around the anal canal to meet those of the opposite side, to become merged in the midline with an aponeurotic thickening. The latter continues to the coccyx, lying beneath the sphincter ani and conforming to its contour (Fig. 9 cf. Figs. 10 and 11).

In the posterior part of the diaphragm, the whole layer of urogenital musculature is laminated, partially separable into strata by complete fascial plates (Fig. 1). Transversely directed fibers of the part of the urogenital diaphragm between the anal and vaginal canals lie just beneath the superficial transverse perineal muscle (Fig. 10); those fibers which pass in exactly transverse course are elevated somewhat on the anterior wall of the anal canal (Fig. 1 level 1); they lie deep to the external anal sphincter and the superficial transverse perineal muscle. From a slightly deeper level appear fascicles which following a more oblique course ultimately reach the sides of the anal canal (Fig. 1 level 2). The coccygeal prolongation of the diaphragm arises from a still deeper level; the fibers, beginning near the tuberosity of the ischium, at first pass medially then, turning posteromedially as they skirt the anal canal, they course toward the coccyx (Fig. 1 level 3). The urethra, then, receives a considerable muscular support on the perineal aspect; sphincter fibers pass into and in front of the urethra (Figs. 9 to 12) downward upon it (Fig. 3, urethra retracted) and behind it (Figs. 1 and 3 at star, mucous membrane removed). The latter band is a reliable for surgical correction of urethrocele

(see Fig. 221 Curtis, 1938). On the pelvic aspect this support is augmented by similar contributions from the pelvic diaphragm, the anterior band of fibers (Fig. 6, at arrow) bounding the inconsiderable perineopelvic hiatus. In some specimens the musculature of the urogenital diaphragm seems to be developmentally defective; the deep compartment containing a venous plexus which is actually bulkier than is its muscular content. Our clinical observations, directed to this feature, indicate that many cases subjected to the rigors of childbearing are predisposed to urethral sagging because the urogenital support is congenitally weak.

The deep layer of the urogenital diaphragm is distinct from the levator ani against which it lies (Fig. 12); there is no intervening fascial stratum between the apposed layers of musculature of the two diaphragms. Although in the middle one-fourths of the width of the urogenital diaphragm in the anovaginal area the anal and urogenital diaphragms are in apposition, fibers are not exchanged between them to a noteworthy degree.

For a discussion of the musculofascial sheaths of the pelvic viscera, which are so important in the repair of cystocele and rectocele, the reader is referred to earlier articles in this series (Curtis, Anson and McVay 1939; Curtis, Anson and Benton, 1940). The current study has impressed the authors forcibly with the importance of the support afforded by the urogenital and pelvic diaphragms in the repair of cystocele and rectocele, reaffirming previous evidence that the musculofascial collars of the viscera are the chief support. Comparison of dissected material with corresponding tissues in patients subjected to cystocele and rectocele operations reveals the fact that there is commonly great hypertrophy of the supporting fascia in pathological cases, the degree of hypertrophy being in general proportional to the duration and extent of the lesion. The urogenital diaphragm and the pubococcygeal part of the pelvic diaphragm play a considerable rôle in the control of incontinence in cystocele cases; transverse mattress suture of the fibers lateral to the floor of the rethra (Fig. 2) is a reliable in all cystocele cases with urinary leakage. In those infrequent cases in which dribbling persists after an apparently successful operation, a satisfactory result may be obtained by bilateral sagging up of the fibers of the pubococcygeus which normally maintain the urethra in close attachment to the pubis (at arrow in Fig. 6 at star in Fig. 13).

In making a lateral or median episiotomy and in the tearing and retraction which accompanies labor the thickenings of both diaphragms are involved

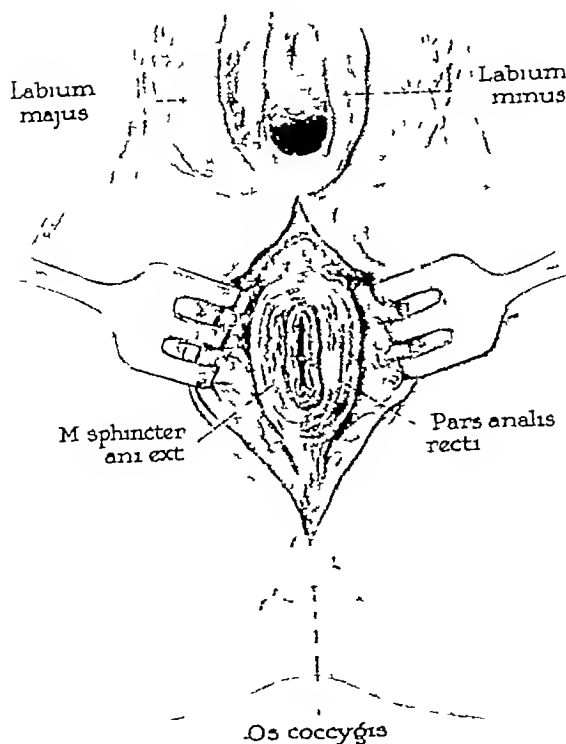


Fig 5 Female perineum, specimen II External anal sphincter, exposed by merely reflecting the skin The position of the coccyx is indicated by dotted line

(Figs 8 to 14) An anatomic feature of clinical importance merits emphasis in this connection, the pelvic and urogenital diaphragms are in close apposition in approximately the median two-fourths of the diameter of the outlet lateralward they diverge greatly, being separated by the anterior recess of the ischiorectal fossa. However, in the entire region subjected to perineal surgery the two diaphragms are in apposition, the urogenital diaphragm comprising perhaps four-fifths of the thickness, the levatores one-fifth. The urogenital diaphragm is more dense and firm, and thicker than the pubococcygeus of the levator ani with which it makes a surgical unit. Together they constitute the so called "levator ani" of clinical parlance.

IV PERINEUM ANAL MUSCULATURE

1 *External anal sphincter* In a perineal approach to the structures which close the pelvic outlet, the external anal sphincter is the first

muscle encountered, it is subcutaneous in position, broad but thin (Figs 5, 8 to 10).

The muscle is an orbicular sphincter, with a prominent coccygeal extension commonly called the anococcygeal ligament. Anteriorly it overlaps the conjoined bulbs of the vestibule, and into it are implanted the small superficial transverse perineal muscles. It is readily dissectable from neighboring structures (Figs 8 and 10). Owing to the proximity of the external anal sphincter to the cutaneous surface, the surgeon has difficulty identifying this structure at operation, further handicapped as he is by retraction of the injured tissues and by pathological changes.

Although a single partial division of the muscle incident to hemorrhoidectomy usually leaves a competent sphincter, a complete tear of the perineum does not, sphincteric incompetence results from retraction of the torn ends of the muscle, and from concurrent tearing of the urogenital diaphragm and the levator ani (Figs 9 to

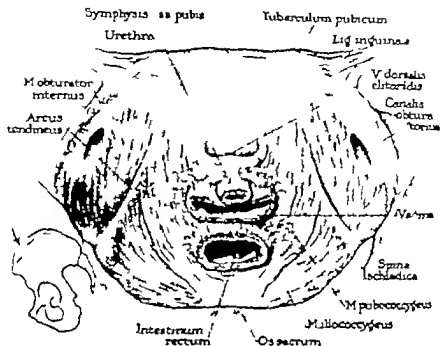


Fig. 6. Female pelvis, specimen III, viewed from above and behind, looking into the lateral anterior portion of the pelvic bowl (see inset arrow indicates direction of view). The musculature is exposed by complete removal of retroperitoneal and ligamentous structures, and of the fascial lining of the pelvis (including the endopelvic fascial continuations upon the sacra). The curved arrow indicates the direction of muscle-fibers in the myofibrillar portion of the pubococcygeus. The urethra, vagina, and rectum have been transected near their points of passage through the pelvic diaphragm. Successive dissections of the same specimen follow (Figs 8 to 5).

2) In the procedure of repair the operative exposure of choice is a preliminary curvilinear incision around the anus, the vaginoperineal flap turned down over the anal aperture, followed by dissection of the retracted tissues, all proportionate to the extent of the lesion. Restoration of the injured sphincter urogenital diaphragm, and levator ani by sutures anterior to the rectum and anus is usually made without identifying the details of each anatomical component, although the circularly disposed firm fibers of the sphincter ani, hidden in the more superficial fibrous and fatty tissues, are in sharp contrast with the bundles of longitudinally directed levator ani at a deeper level closely applied to the rectal core

pelvic peritoneum and subserous tissues was fully described. It was therein stated that the general cellular tissue, the heavy ligamentous support of organs, and the fascial tubes covering the latter may be even more readily mobilized by gross dissection than they usually are in the course of pelvic surgery even by those who employ the technique of scissors dissection. Of these various tissues, contrary to Tandler's belief (in *Arch Stoeckel*) clinical evidence substantiated by anatomic dissection indicates that the peritoneum serves not merely as covering but that, with the contiguous areolar tissue attached thereto, it affords real support.

V. PELVIS PERITONEUM AND SUPERITONEAL TISSUES

In an earlier article in this journal (Curtis, Anson and Beaton 1949) the anatomy of the

VI. PELVIS PARCI A. MUSCULATURE

1. *Endopelvic fascia* That part of the endopelvic fascia which is reflected upward upon the rectum and vagina leaves the pelvic floor at the points at which these organs pass through the

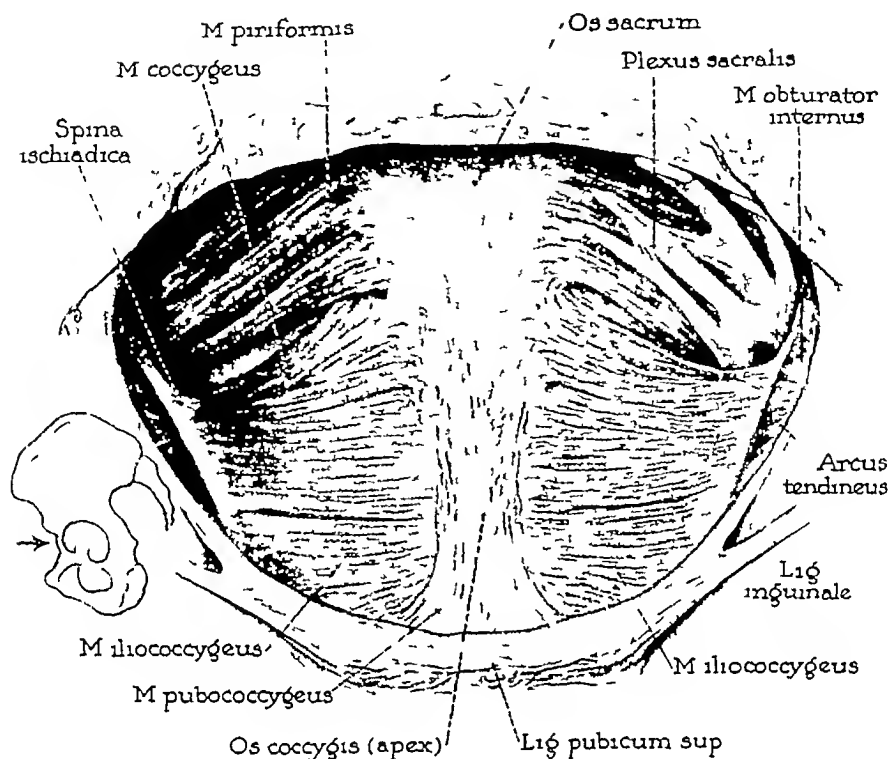


Fig 7 The same specimen, viewed from the front, looking into the "parietal," or posterior, part of the pelvic bowl (see inset) Dissection as in preceding figure

diaphragmatic musculature (Curtis, Anson, and McVay, 1939, Figs 1 and 2) The covering for the bladder, however, is reflected away from the inferolateral walls of that organ in such a way that the urethra receives only a partial investment, being so covered only in front Since there are three tubes of fascia, in succession, encasing the urethra and bladder, the vagina and lower uterus, and the rectum, there is a double layer of fascia between adjacent organs In each instance the fascial sheath is in intimate relationship with the musculature of the corresponding viscus, receiving muscle fibers from it The fascial sheaths, each re-enforced by muscle fibers from the subjacent coat of smooth muscle, are utilized to furnish the major support in the repair of herniations of the tubular viscera, i.e., urethrocele, cystocele, and rectocele (Particularly in the case of rectocele, and in cystocele with incontinence, repair of the levator ani and the urogenital diaphragm are also important)

There has been prolonged controversy as to whether the supporting tissue utilized in plastic repair is muscle or connective tissue, likewise, it has been emphasized by anatomists that there is no fascial tissue in these regions sufficiently extensive or firm enough to be of service in repair A simple explanation suffices Wherever there is unusual mobility, also under pathological conditions, such as uterine prolapse or cystocele, there are always localized thickenings of the connective tissue This accounts for anatomists' failure to discover the thick vesicovaginal supportive tissues, an "anatomists' oversight" which aroused Halban's curiosity Blair Bell's academic insistence that the supportive tissue is muscle, not fascia, meets explanation in the fact that the fascial sheaths derive muscle fibers from the hollow viscera which they surround Here, too, we meet Tandler's requirement that connective tissue must be associated with muscle in order to be classified as "fascia" and in order to yield real

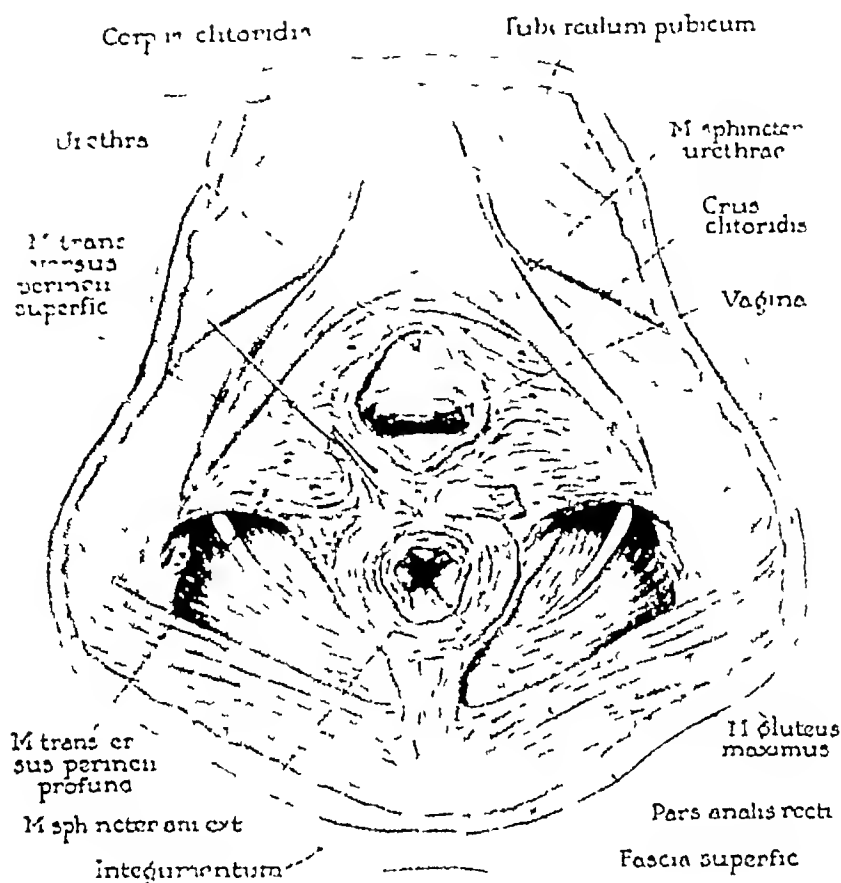


Fig. 6. In the anal triangle the external anal sphincter has been freed somewhat in order to show the coccygeal extension of the urogenital diaphragm. In the urogenital triangle the following superficial structures of the perineum have been removed: the integument and the subcutaneous tissue; the mucous membrane of the vestibular walls; the vestibular bulbus (no intermediate mass present); the inferior fascia of the urogenital diaphragm; some of the more superficial fibers of the urethral sphincter and deep transverse muscles which were attached to the inferior fascia. Shown are the following: the muscles of the urogenital diaphragm, roof of the vestibule, with the vaginal and urethral orifices; a portion of the transverse ligament of the pelvis; the body of the clitoris; the inferior perineal fascia as it invests the ischio-cavernosus muscles and covers the front of the pubis; the medial portion of the superficial transverse perineal muscles (stump on left elevated to demonstrate fusion at the central tendinous point of the perineum). The transverse ligament of the pelvis (i.e., the anteriorly fused fascial layers of the urogenital diaphragm) is concealed by the pubic symphysis.

has been removed, the musculature is brought into view (Figs 6 and 7). The muscles are disposed in two pairs, levatores ani and coccygei. The levatores occupy chiefly that part of the pelvic outlet anterior to coccyx, the coccygei that portion of the outlet behind (and above) the terminal elements in the vertebral column (Fig 7, cf Figs 14 and 15). Together they form a supporting floor upon which the pelvic viscera rest

and in which their terminal portions are firmly anchored (Fig 6), also a dorsal wall for the pelvic cavity (Fig 7). Each levator ani consists, in turn, of two parts, pubococcygeal and iliococcygeal, which, respectively, serve in the capacities just mentioned. These subdivisions will now be discussed separately, as will also the piriformis and obturator internus muscles which assist in forming the lateral and dorsal walls of the pelvis.

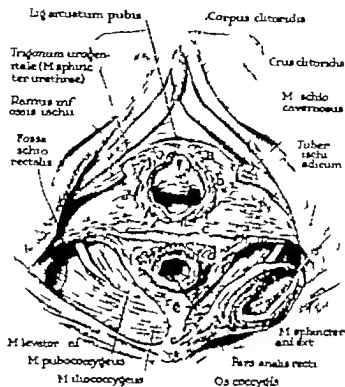


FIG. 1. In the anal triangle the external anal sphincter, now detached from the subjacent muscles of the ischioanal and pelvic diaphragms and from the intrinsic musculature of the anal canal, has been dissected aside to reveal the back- and directed fibers of the ischioanal triangle, the ischio-cavernosus muscles have been rolled medialward away from the crus and the body of the clitoris; the superficial transverse perineal muscles have now been entirely removed to show the course of fibers to the base of the ischioanal diaphragm. It is evident that the so-called sphincter of the urethra sends muscle fibers not only into and in front of the urethra, i. e., but also into the vagina, & across the midline between the vagina and anus, but the all of the latter & and back and to the coccyx.

a. P. pubococcygeus muscle. The pubococcygeal muscle is, obstetrically and surgically, the most important muscular element of the pelvic diaphragm, since it serves as a direct support for the bladder and urethra, for the vagina and uterus and for the rectum. This fact is not made clear in the accounts presented in either surgical or anatomical textbooks; on the contrary, it is everywhere figured as sweeping backward around the organs to leave a very considerable opening in the anterior half of the pelvic diaphragm.

Viewed from within the abdomen (Fig. 6) the pubococcygeal portion of the levator ani is seen to be attached along the pubic bone and the

tendinous arch, the latter being the longer organ, the junction of the two forming a peak directed forward. Anteriorly there is merely a shallow hiatus, not a U-shaped cleft. In the midline the dorsal run of the clitoris passes through this opening into the pelvis, behind the pubic arcuate ligament and in front of the transverse ligament of the pelvis. The anterior fibers which cross transversely in front of the urethra are muscular and form a narrow but strong band; those nearest the urethra ascend upon the latter as do others from the lateral aspect. Some fibers also descend upon the urethra. The cleft is not seen in perineal view, being concealed by the inferior por-

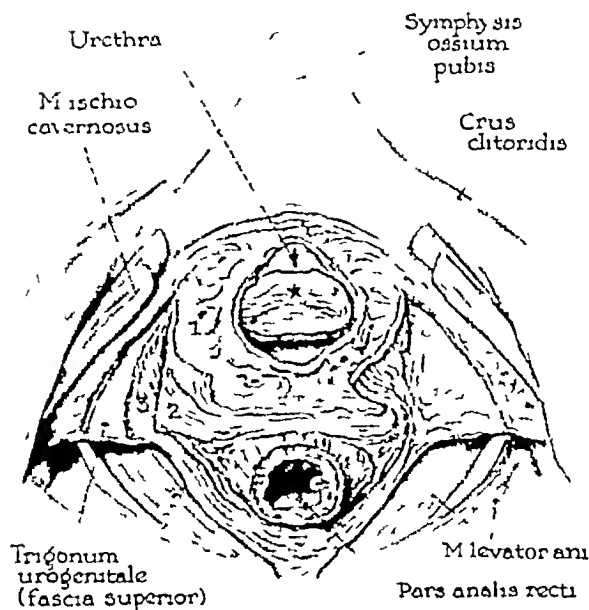


FIG. 11. In the anal part of the perineum the structures remain as in the preceding drawing. In the urogenital part of the perineum on the right the musculature is reflected as a single sheet to expose the superior fascia of the diaphragm, on the left its laminated character is demonstrated by making a similar elongate cut, but to depths which mark natural cleavage planes along which the strata are freed for a short distance to either side of the incision. The superficial lamina, 1, passes chiefly to the vagina, the intermediate one, 2, into and in front of the anal canal, the deep layer, 3, backward to the coccyx. The body of the clitoris and the anterior portions of the crura have been removed, the ischiocavernosus remain only at their proximal ends. The mucous membrane has been removed on the anterior wall of the vagina (at star) to show the muscular support derived from the urogenital diaphragm.

tion of the pubis (Figs 10 to 12). As may be seen from within the pelvis, the "visceral" sets of fibers of the pelvic diaphragm turn quite directly toward each organ, gaining implantation into their walls (Fig 6). The anterior cleft, then, is very shallow—not evident at all in perineal view (Fig 9). The urethra is firmly attached to the pubis—a fact of major clinical importance.

In the excavation between the vagina and rectum the narrow anteroposterior band of fibers fastens the organs closely together and ascends upon each tube. Behind the anal canal, many pubococcygeal fibers follow a semilunar course, but the majority pass posteriorly, in a thin sheet, to the coccyx, resting upon the iliococcygeus (Fig 6, concealed by the latter in pelvic view, Fig 12).

b Iliococcygeus muscle. The arciform aponeurotic origin of the iliococcygeus is shared with

that of the pubococcygeus (Fig 6, Figs 14 and 15, observer's left half of figure). The direction of the fibers is transverse (Fig 7), in contrast with the arrangement of fascicles in the pubococcygeus, whose fibers are directed somewhat sagittally (Fig 6).

c Coccygeus, piriformis and obturator muscles. The pelvic diaphragm is completed on each side posteriorly by a coccygeus muscle (Figs 7, 14, and 15). The plane of the flat surface of the coccygeus muscle lies at almost a right angle to that of the iliococcygeus. Narrower at the origin than at the insertion, in contrast with the iliococcygeus, the paired muscles fill the space between the iliococcygeus and the piriformis. The fibers of the coccygei do not unite in the midline in a muscular band but are inserted almost entirely into the coccyx by a firm thin aponeurosis.

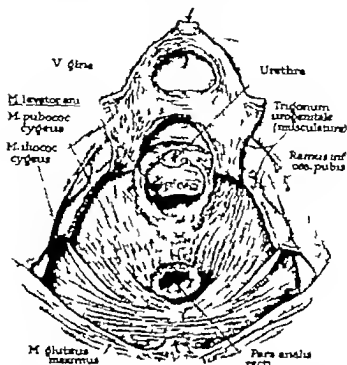


Fig. 2. The urogenital diaphragm has been freed from the pelvic diaphragm, cut along the ischio-spiral ramus on each side and the coccygeal part behind (see arrow) then turned forward on the remaining pelvic attachments. The space thus opened into is the anterior recess of the ischio-rectal fossa, from which all fatty tissue has been removed. The pubococcygeal part of the levator ani, exposed by removal of its thin resting lamina, is shown to constitute supporting muscle sheath for each of the lateral tubes.

The piriformis muscle partially closes the space of the greater sciatic foramen (Figs. 14 and 15) although belonging to the psoas-femoral group of muscles (like the obturator internus) it serves, to a degree, a diaphragmatic function, since it continues in the stratum of the coccygeus. In the standing position, the muscle is on the wall rather than on the floor of the pelvic cavity.

The importance of the obturator muscle as a parietal element is emphasized by examination of the space which it occupies (Fig. 4, cf. Figs. 6 and 15). The obturator internus fills the lesser sciatic foramen as it passes through the foramen.

3. *Pelvic diaphragm as a whole.* The three muscles which constitute the pelvic diaphragm proper and which represent the original tail muscles, *i. e.*, the pubococcygeus, the ilio-coccygeus, and the coccygeus, all take origin from the pelvic bones. The parts of the levator are either implanted into the walls of the tubular organs for

which they constitute a diaphragmatic support or—in the intervals between adjacent organs and in those between organ and bone—join the corresponding muscle. The opposite half of the pelvis. The coccygeus, being posteriorly situated, must insert into the sides of the coccyx. In the specimens illustrated a distinct cleft separates the adjacent muscles of the diaphragm, as is apparent when the *in resting laminae* are removed (Figs. 14 and 15).

The pubococcygeal portion of the levator ani constitutes what might be termed the "visceral" part of the pelvic diaphragm, since it is by this muscle that the terminal portions of the lateral tubes are firmly clasped (Fig. 6). There is no "hiatus of the levator ani" surrounding the visceral tubes at the site of their perforation of the pelvic diaphragm (Figs. 6, 14, and 15) the implantation of the medial fibers of the pubococcygeus firmly into the viscera constitutes a

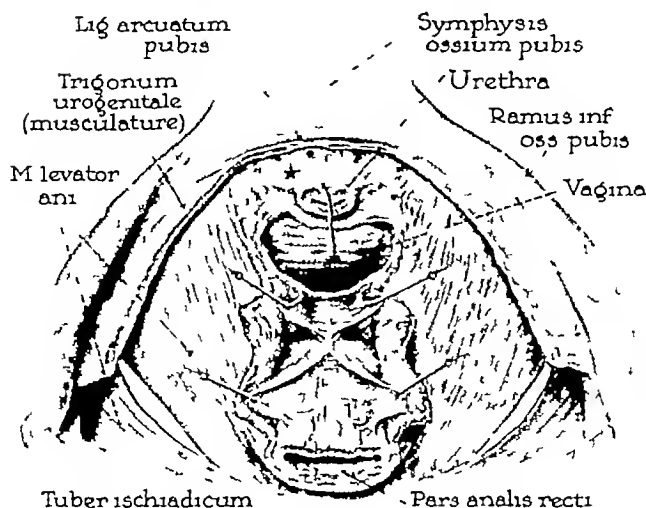


Fig 13 The urogenital diaphragm has been removed except for a narrow strip of attachment along the ischiopubic rami and at the transverse ligament of the pelvis. Here are exposed the components of the clinically important "perineal wedge", the pelvic diaphragm has been incised in the middle line from the anal to the vaginal canal. The relation of these canals to the pelvic diaphragm and to fascial sheaths which intervene between pelvic diaphragmatic and intrinsic layers of musculature is shown. Like the vagina and the anal part of the rectum, the urethra receives special fibers from the levator ani (see star).

firm attachment. In perineal view it may be seen that the fibers which reach the sides of the anal canal descend upon it, as if interrupted in their course, as they descend, their direction is slightly backward as well as toward the surface (Figs 12 to 15). The fibers which reach the front of the canal likewise descend upon it, forming with the others a sleeve of definitely funnel-shaped character. More medially placed fibers, which, similarly, reach the vagina, terminate upon its sides, without, however, turning sharply inward (i.e., without changing course from sagittal to coronal plane), they fade away as they approach and interweave with the intrinsic muscle fibers of the vagina.

The intimate relationship of the pubococcygeus to the visceral tubes, and the direct support which this arrangement affords (Figs 6, 13, to 15), are of fundamental importance in a proper understanding of the mechanics of plastic repair. Yet the operator should be aware that this muscle is in relation only with the terminal portions of the viscera, the support at a higher level is contributed largely by the fascial collars and related ligamentous structures. The latter statement applies particularly to the operative relief of

cystocele and urethrocele, adequate rectocele repair requires not only the support of the rectovaginal fascial sheaths, but also restitution of the pubococcygeus together with the urogenital diaphragm.

Contrary to the usual gynecological concept, the chief part of the pelvic diaphragm is centered farther posteriorly than clinicians are accustomed to consider it. The bands of muscle fibers constituting the diaphragm are less massive anteriorly, in the urogenital region, becoming more dense and concentrated posteriorly where the fibers converge behind the rectum. The heavier nature of this so-called "levator plate" is ascribable to the fact that the fibers of the iliococcygeus course more transversely than do the fibers of the pubococcygeus, therefore, as the two subdivisions of the levator ani approach the coccyx, there is a double muscular banding where the iliococcygeus passes beneath the V-shaped vertebral extension of the pubococcygeus (Fig 6, cf Fig 14). Nor is this all, since beneath the former, in turn, is situated the conjoined muscular plate consisting of the external anal sphincter and the coccygeal prolongation of the urogenital musculature (Figs 9 to 11). The iliococcygeus is thus clasped be-

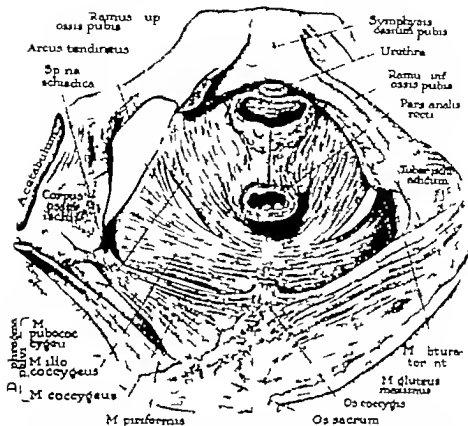


Fig. 14. Portions of the right hemipelvis have been removed (cut through the inferior pubic ramus near the symphysis and the ischium superior to the level of the spine) to demonstrate the attachments, form and relationships of the pelvic diaphragm. The following features are especially important: the clefts between the adjacent muscular elements of the pelvic diaphragm, tendinous origin of the pubococcygeal and iliococcygeal divisions of the levator and the manner in which the pelvic passes deep to the iliac division, the proximity of the urethra to the pubic symphysis, and the greater distance between vagina and anus; the complementary position which the coccyx holds to the ilio-coccygeus (left), the manner in which it is covered by the gluteus maximus (right); the dorsal situation of the perforators.

tween two musculoaponeurotic plates, each a dorsally directed appendage of a diaphragm; the superior one of the two (the pubococcygeus) supports the visceral tubes on their pelvic aspects (Fig. 6); the inferior (the so-called urethral sphincter strengthened by the anal sphincter) contributing levator support on the perineal side (Fig. 9).

This means that the area of the so-called "anococcygeal body" is one in which the constituent layers are readily separable and in which indiscriminate surgery might destroy important supporting elements. Described usually in reference to the related portion of the colon, it is said

that the levatores "meet each other posteriorly in the anococcygeal body," "a fibromuscular body mingled with fat" and "placed between the anal canal and the tip of the coccyx" (Cunningham). Actually, as described above, this is not an area where tissues are mixed without semblance of physical plan; coccygeal insertions, arranged in lamellar fashion, provide vertebral fixation for diaphragmatic and sphincteric musculature (Figs. 9 & 11).

The "perineal body" is likewise described in the standard accounts as an "indefinite mass" situated between the anal canal and the vagina. Its muscular constituents, however, are listed—then

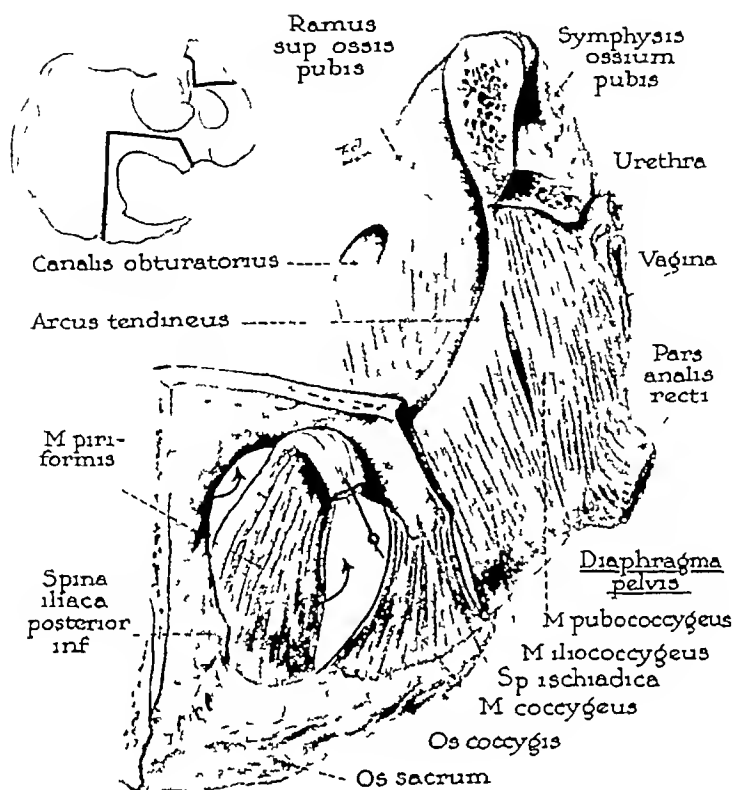


Fig 15 Pelvic diaphragmatic and associated musculature Lateral view By cutting parasagittally through the superior pubic ramus and through the body of the ischium in front of the spine, and by then removing the bone between the pubic and ischial attachments of the levator ani (see inset), the following additional anatomical features, important in gynecology, are demonstrated the arciform origin of the levator ani from the covering of the obturator internus (latter intact on specimen's left half), the uniformity in direction of the levator fibers the position of the anal part of the rectum at the "spout" of the diaphragmatic "funnel", the capaciousness of the foramina above and below the piriformis (at arrows), the relatively small size of the clefts between parts of the diaphragmatic musculature, the depth of the bony sciatic notch which is closed by the coccygeus and piriformis muscles

being the anal levator and sphincter, the bulbocavernosus and transverse perineal muscles (cf Figs 9 to 11). The collection is said to be a wedge-shaped mass, the edge of which is directed upward, the base downward toward the skin. It is a matter of surgical consequence that the apical part of the wedge consists of the pubococcygeus muscle (Fig 12), and, more deeply, of the fascial coverings of the anal and vaginal canals (Fig 13). If this succession were not appreciated, repair of rectocele could not be properly managed nor dangerous instrumentation within the pelvic cellular tissues fully avoided.

The iliococcygeus has no direct relation to the organs as they pass from the pelvis to the exterior, even its most anterior fibers are removed from the anal canal by an appreciable distance, in crossing the midline in front of the coccyx, the muscle merely forms part of the floor and wall upon and against which the terminal part of the rectum rests. Similarly, of course, the iliococcygeus offers indirect support to the sigmoid colon and the jejunoleum, especially when the body is in the standing position. The iliococcygeus is of obstetrical importance as a support, it is of lesser interest in gynecological plastic operations. As

part of the pelvic diaphragm. It is a factor in uterine support, and it is also important clinically in relation to disturbances in function of the sigmoid-rectum, which it supports to varying degree in different individuals.

The coccygeus is of subsidiary diaphragmatic service in helping to support the organs as they lie within the pelvic cavity and in passing as a band-like barrier across the space between the coccyx and the ischial spine. It assists the levator ani (Figs. 7, 14 and 15). In pregnancy it furnishes a major support, but in labor although subject to considerable strain, it forms only the posterior wall of the parturient canal and therefore suffers material injury only in pathological cases.

The coccygeus, piriformis, and obturator internus muscles assist the associated ligaments in maintaining the integrity of the sacroiliac joints holding the posterior wall of the pelvis together. Important anatomically as part of the pelvic framework, they are of gynecologic importance chiefly in relation to backache and sacroiliac sprain.

As mentioned above, the retropublic cleft transmits the dorsal vein of the clitoris (Fig. 6) and not infrequently an accessory clitoral artery. This transmission brings into vascular communication, by an anterior route, the pelvic and perineal tissues. The sciatic foramina transmit the internal pudendal vessels (cut in Figs. 8 and 9) serving a comparable function posteriorly. There are however intermediate vascular connections of lesser importance. In specimen III passing from the deep surface of the vestibular bulbs, they are carried through minute openings in the urogenital (Figs. 10 and 11) and in the pelvic diaphragm (Fig. 13) they are grouped around the anal canal, and occur only in that median area where the two diaphragms are in contact; they are not situated in a lateral position where their route would involve passage through an ischio-rectal fossa. Whenever vessels are not confined to the two main pudendal routes (retropubic cleft and sciatic foramen) they are concentrated as accessories, in a median swath some two-fifths the width of the pelvic outlet. Curiously vessels do not employ in their perineopelvic passage the clefts which separate the three subdivisions of the pelvic diaphragm (pubococcygeus, ilcococcygeus, and coccygeus muscles).

SUMMARY AND DEDUCTIONS

The subcutaneous tissue of the labium is not an indiscriminate mass of fatty tissue through which pass scattered fascicles of dartos muscle. It is a definitely lamellated stratum in which is lodged a

finger-shaped fatty diverticulum of the superficial inguinal fascia which is readily shelled out of its labial pocket. It is this process which produces the mound-like form of the greater lip. The posterior limit of the labial mound is coterminous with the bluntly pointed tip of the prolongation. The process rests upon the deep membranous layer of the superficial fascia. Within the tissue of its proximal portion, which begins at the subcutaneous orifice of the inguinal canal, not only is the round ligament dissectable but also is thinned form successively the labial extensions of the parietal layers of the abdomen.

Within the perineal compartment for which the deep membranous layer of fascia forms a firm floor a much thinner but clearly defined layer the inferior perineal fascia covers the bulbocavernosus and ischio-cavernosus muscles, the former again invested with a firm musculofascial sheath. In addition to the very definite individuality of its layers, another feature of the perineal fascia merits clinical as well as anatomical emphasis: the firm musculofascial sheath which overlies the bulbocavernosus muscle assumedly is that utilized in the operation of M'artius, a procedure for relief of incontinence of urine in cases with destruction of the floor of the urethra.

Inability to palpate the normal Bartholin gland is not ascribable solely to its small size (Fig. 4). It lies hidden behind the fatty process at a considerably lower level than the infected gland, which is limited posteriorly by firm musculofascial tissues and therefore must extend anteriorly as it enlarges.

The proximity of the external anal sphincter to the cutaneous surface merits emphasis, as do also its wide trigonal and coccygeal attachments. In operative restitution of the sphincter the firm anal and coccygeal extensions of the urogenital diaphragm and the pubococcygeal part of the pelvic diaphragm are important factors in the repair.

At the central tendinous point of the perineum the anal sphincter blends with the superficial transverse perineal muscle. The transverse perineal muscle in turn, is blended with the underlying musculature of the urogenital diaphragm. The latter does not end at what is commonly considered the base of the urogenital diaphragm. Rather it is prolonged to coccygeal insertion, the urogenital diaphragm constituting totally a sling which utilizes not only pubis and ischium for fixation, but also the end of the vertebral column.

The muscular roof of the urogenital diaphragm is trifoliate. Strictly it is the deepest of the three

laminae of the urogenital diaphragm that end on the coccyx, the intermediate one surrounds the anal canal, the most superficial merges chiefly with the walls of the vagina and the urethra and the anterior portion of the external anal sphincter.

We have been taught, catechetically, that the urogenital musculature crosses the midline between urethra and vagina, and between vagina and rectum, but that the pelvic diaphragm is deficient in relation to the visceral tubes, fibers supposedly sweeping backward behind the anal canal, to leave an elongate U-shaped cleft, but such a concept is entirely incorrect, fibers of the pubococcygeal part of the levator ani reach each of the three tubes—anal, vaginal, and urethral, and descend upon each to blend with the intrinsic muscular coat. The visceral support is so complete that even the urethra receives a full investment, no cleft is visible from the perineal aspect, even when the urethra is drawn away from the pubic symphysis.

It is the anterior or pubococcygeal division of the levator ani that affords continuous support for the organs of the urogenital and pelvic parts of the perineum, the iliococcygeus completes the diaphragm at the sides and behind, but does not come into contact with the viscera. It underlies the coccygeal extension of the pubococcygeus. This reduplication of muscle layers gives added firmness to the so called levator plate, that heavy

portion of the levator ani situated behind the anus.

The preurethral cleft is small, oval in outline, little more than a retropubic hiatus for transmission of vessels and nerves from perineum to pelvis. Normally the urethra is close to the pubis—a fact of clinical importance in evaluating lesions associated with incontinence of urine. The urethra is displaced from the pubis by a traumatic labor, the pubococcygeal anchorage to the pubis being thereby disturbed. It is this preurethral cleft anteriorly and the sciatic foramina posteriorly that transmit almost all of the important blood vessels from one side of the pelvic diaphragm to the other.

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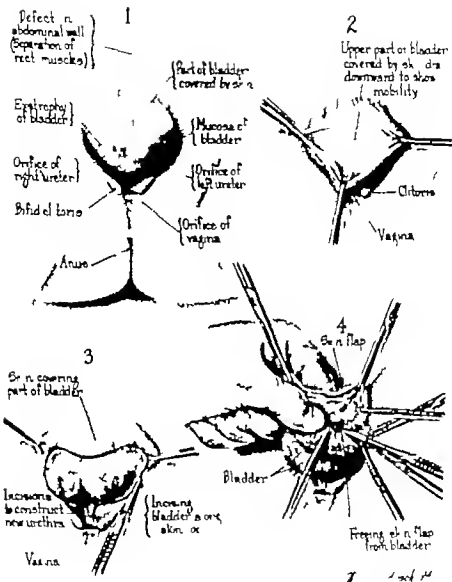


Fig. 3. Condition present at beginning of operation. Skin had grown down over upper half of bladder. This, as well as flap, which greatly facilitated covering over. Inset 3 shows line of incisions and the strip of mucous membrane which provided tissue to form the urethra. Details are shown of technique by which excess skin and mucous membrane around urethral neck and urethra were excised, and then urethra formed, bladder closed after insertion of U-shaped duct which emerged below.

EXSTROPHY OF THE BLADDER

The First Case in Which a Normal Bladder and Urinary Control Have Been Obtained by Plastic Operations

HUGH H. YOUNG, M.D., F.A.C.S., Baltimore, Maryland

OF ALL genital abnormalities exstrophy of the bladder is certainly one of the most terrible. Until the recent present no operator has, I believe, ever obtained a complete cure in exstrophy. The great Iren delenburg spent his life trying to get a perfect result in these poor children and shortly before his death, in a very frank and pathetic article, he detailed the many variations of technique that he had employed without a single perfect result. He believed that it was necessary to disarticulate the pelvic bones at the sacroiliac synchondrosis so as to bring the widely separated pubic bones together in order to get a satisfactory urethra with sphincteric control but even though he carried out this osteoplastic technique and succeeded in turning in the exstrophic bladder he failed to get urinary control in a single case.

I too have been working on this subject many years and although on the verge of success several times, some complication has always occurred to prevent a complete cure of the exstrophy with perfect urinary control and interval urination. After a series of these heart-breaking failures I am glad to be able to report a complete success in a case of extensive exstrophy of the bladder in a girl of 6 years in whom, by a technique that I have gradually developed, I have finally succeeded in obtaining the cure of this awful affliction that

From the James Buchanan Brady Urological Institute, Johns Hopkins Hospital.



Fig. 1. Photograph of patient at age of 4½ years. Exstrophied bladder is 2 inches in diameter.

has been sought for by surgeons the world over for many, many years.

CASE REPORT

Extensive exstrophy of the bladder with 4 inch separation of the pubic bones. Cure of exstrophy at first operation, urinary control obtained by urethral and muscle plastic at second operation.

I. T., a girl aged 4 years, was admitted to the Brady Urological Institute on June 15, 1939 with congenital exstrophy of the bladder. Her faithful mother, by dint of great care and cleanliness, prevented inflammatory complications but the large extruded mass and the constant escape of urine into the child's clothes made life unbearable. Otherwise the child had developed well and enjoyed excellent health. The condition present is shown in Figure 1. On the surface of the exstrophied bladder two cone-like projections were present and from them urine spurted on each side. A roentgenogram showed wide separation of the



Fig. 2. Plain x-ray film showing wide separation of pubic bones (10 cm). Outlines of round exstrophied mass are shown.

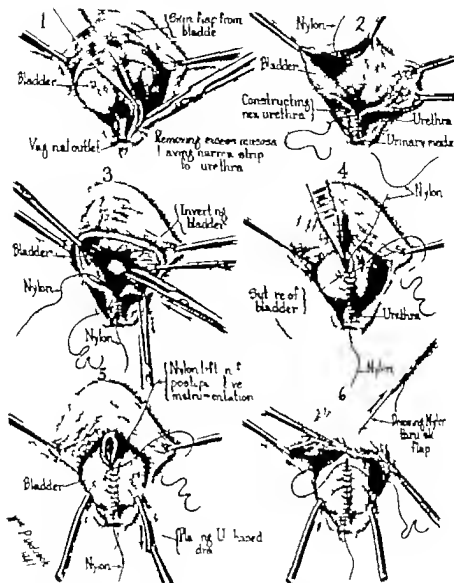


Fig. 4. Plastic to form urethra, replace bladder within abdomen, and close it after supplying U shaped catheter drains.

pubic bones with ligament connecting them. On this lay the wide open urethra. The mother, as instructed, to redouble her efforts to prevent inflammatory changes in the entrophied mucosa and to return with the child in a year for operation.

On July 2, 1940, the patient returned. With the child standing the entrophy presented large almost globular masses which had increased in size and projected inches from the surrounding abdomen. In the recumbent position the entrophied bladder measured inches in diameter. The ureters were seen as bulging prominences on each side

of the lower third. The upper half of the entrophied mass was covered by epidermis. The covering of the rest of the bladder looked like a normal mucous membrane. The line of demarcation between the skin and the mucosa was sharp. The urethra was wide open and contained central rib. The orifice of duct, probably Bartholin's, was visible on the left side. The clitoris was divided and presented rounded areas on each side (Fig. 5). The orifice of the vagina as small traces were slit. The perineum and anus appeared normal. The entrophied mass was easily pushed with finger back through an opening in the abdominal

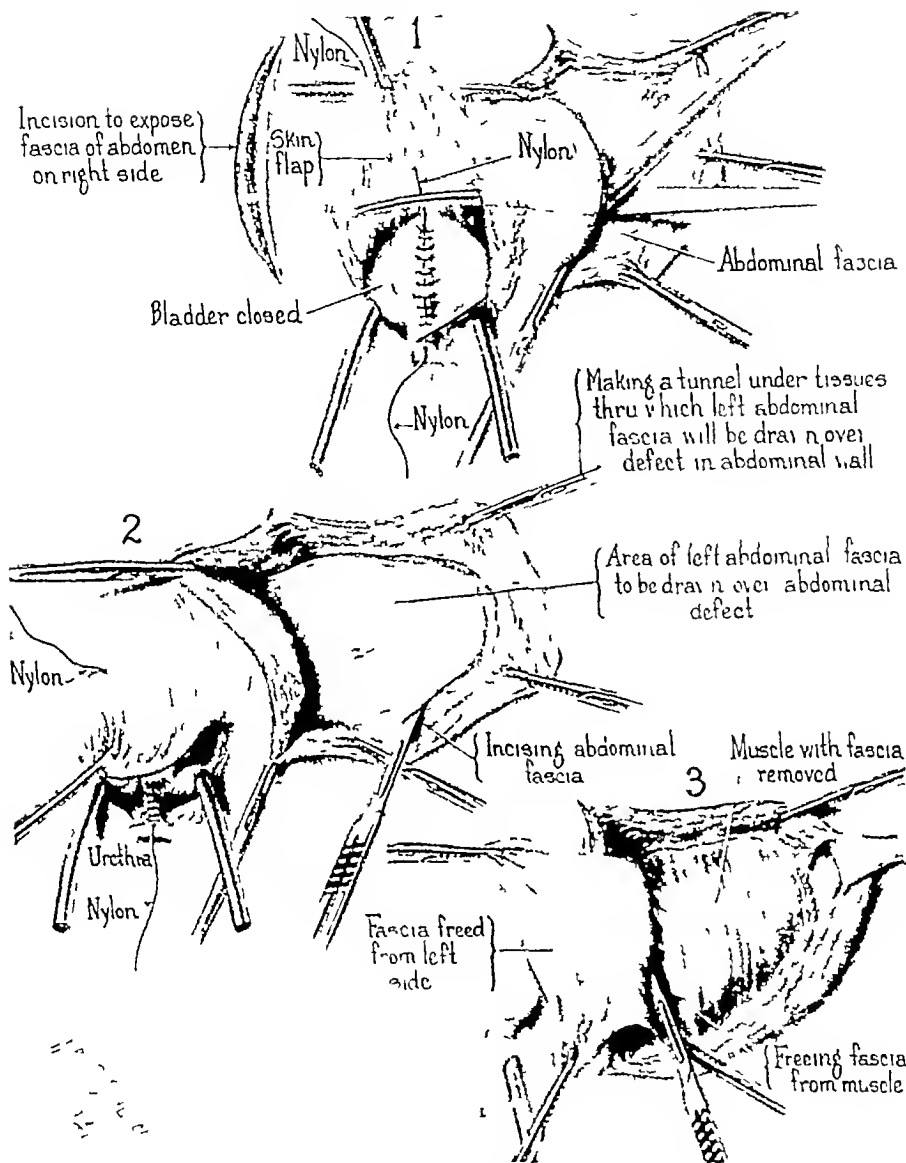


Fig. 5. Technique employed in obtaining fascial transplants from abdomen

wall which had solid firm edges. External to these the widely separated recti muscles ran downward and outward to join the separated pubes. With the exception of the central defect the abdominal musculature appeared normal. Streams of urine escaped intermittently from the ureters. Urine collected from both sides was pale of low specific gravity and free from infection. General physical examination was negative.

A plain x-ray negative (Fig. 6) showed a 10 centimeter separation of the two halves of the pubes. The globular extroploded mass was plainly shown.

Mr. Ditsch's drawings depict the condition and the operative technique accurately.

In Figure 3, 1, the skin which covers the upper half of the exstrophy is shown and below it the orifices of the ureters, the wide open urethra, the separated halves of the clitoris, and the orifice of the vagina. In Figure 3, 2, clips placed on the skin at its juncture with the vesical mucosa demonstrate, by traction, that this skin can be used to cover the wound at operation. The incision crossed at the junction of the skin and mucosa and then continued around the exstro-

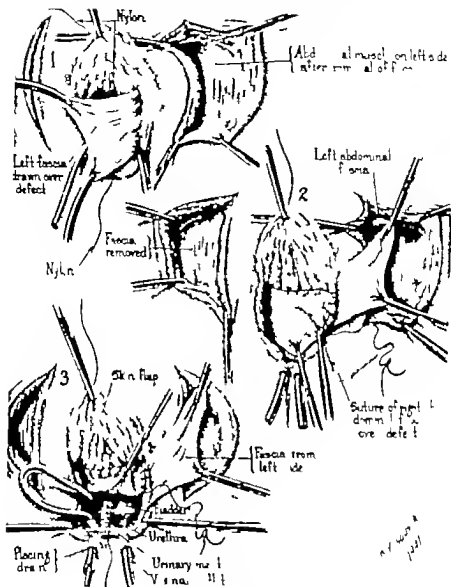


Fig. 6. Fiber details of fascial transplantation. Tissue strength fascia from both sides as employed.

phed bladder and down below to form new urethra (Fig. 3, 3). In Figure 3, 4, the skin flap is being dissected from the bladder muscle. Figure 4, 1 shows the excision of mucosa on each side of the urethral flap thus disclosing muscle to be used in forming a sphincter. In Figure 4, 2 the edges of the mucosa are approximated with a continuous No. 00000 chromic catgut suture thread of 10 in being left in the new made urethra as

subsequent conductor. In Figure 4, 3, the bladder is pushed through the abdominal defect preparatory to approximating the sides of the bladder wall (Fig. 4, 4). Drainage is provided with a rubber tube which in the form of a U emerges from the bladder on each side (Fig. 4, 5). In Figure 4, 6 the bladder closure has been completed, and the nylon is brought out through puncture of the skin flap. Having closed the urethra and bladder

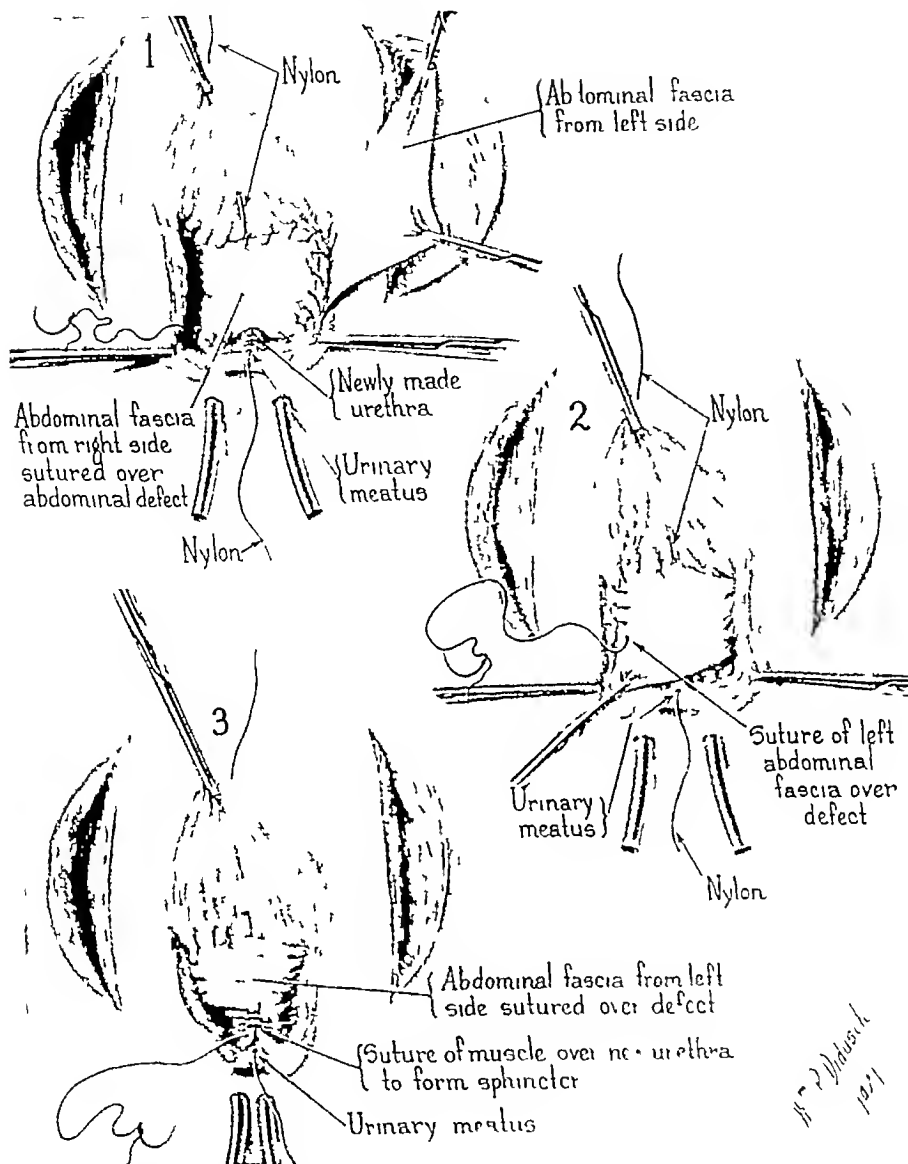


Fig 7 Suture of fascial transplants completed (insets 1, 2) after which U shaped tubes had been drawn out along side of thigh for vesical drainage Inset 3, Muscle drawn over new made urethra

the next step provides fascia to close the defect between the recti muscles. This technique is shown in Figure 5. In 1 the incisions are made on each side to expose the abdominal fascia. On the left side the wound has been retracted, thus exposing abdominal fascia which is freed from superimposed skin and subcutaneous tissues along the side of the exstrophy. A tunnel is made here and is enlarged by spreading a clamp, as shown

The incision is made through the fascia as shown in Figure 5, 2. By blunt and sharp dissection the fascia is separated from the overlying abdominal muscles (Fig 5, 3) up to the edge of the abdominal defect. In Figure 6, 1, this strip of fascia has been drawn through the opening over the inverted bladder. On examination it seemed that this strip of fascia was hardly large enough in itself, and it was decided to obtain another similar

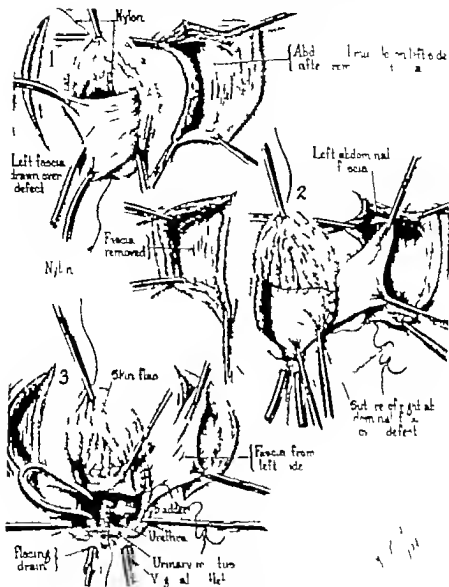


Fig. 6. Further details of fascial transposition. T-tissue strength fascia from both sides as employed.

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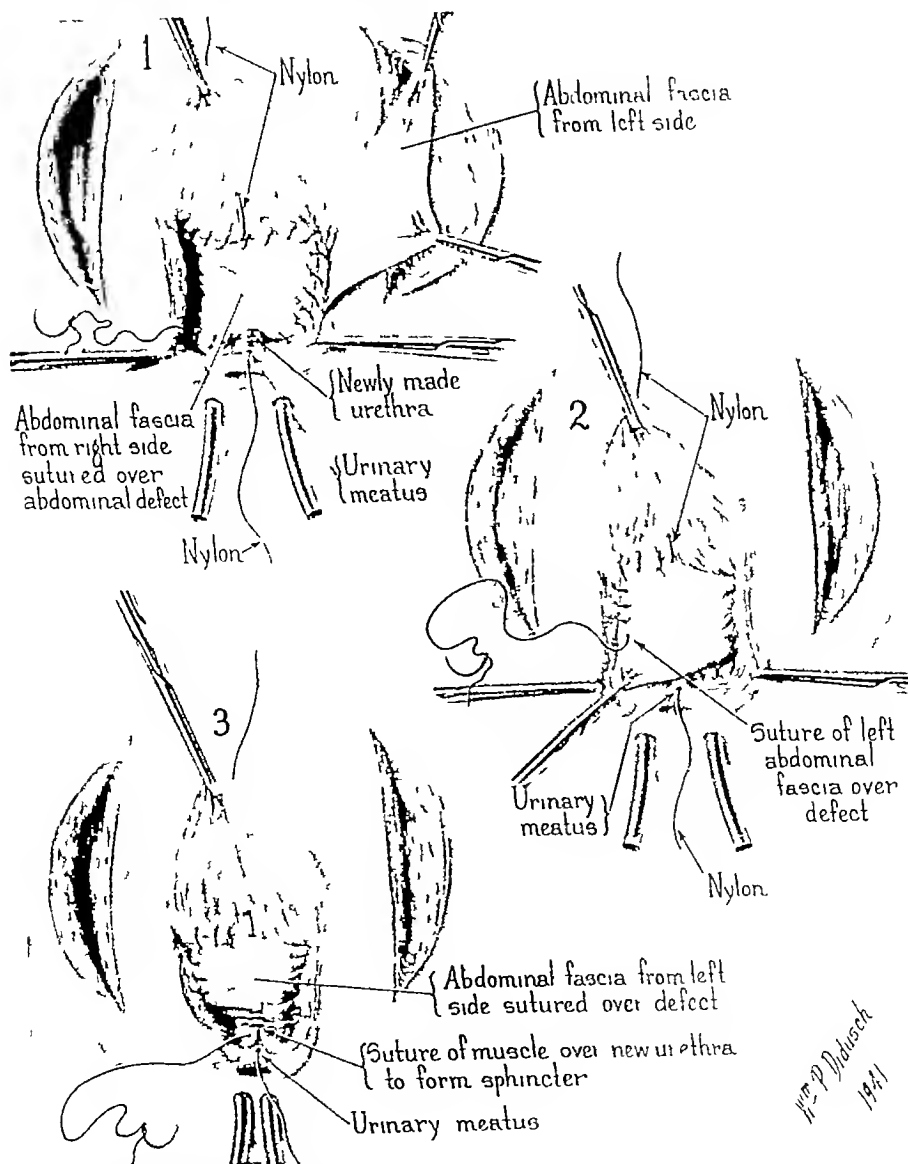


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W. P. Dicksch
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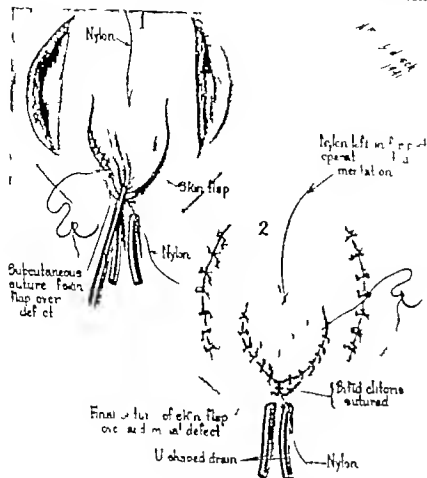


Fig. 8. Covering of deep plastic procedure upon bladder and urethra with an oval flap of skin which previously, as dissected from upper half of bladder.



Fig. 9. Appearance on return of patient 6 months later. Ectrophy cured. Patient voiding through urethra but urinary control imperfect—partial incontinence.

strip from the right side as shown in Figure 6, 2, in which the fascia has been drawn across and sutured to the edges of the abdominal defect, thus completely covering the bladder. Before the lower sutures are placed the U shaped catheter which has been inserted into the bladder for drainage, is carried beneath the pubic ligament and skin, on each side of the vagina, so as to emerge through the skin of the upper part of the thigh, as shown in Figure 6, 3. In Figure 7, 1, suturing of the abdominal fascia from the right side is completed. The left is held ready to be applied over it, as shown in Figure 7, 2. The next step is to cover the new made urethra with muscle drawn from each side. The technique is shown in Figure 7, 3. The orifice of the urethra with the fascia above it and the two rubber drains emerging from the wounds of the thighs are depicted. The oval skin flap which has been dissected from

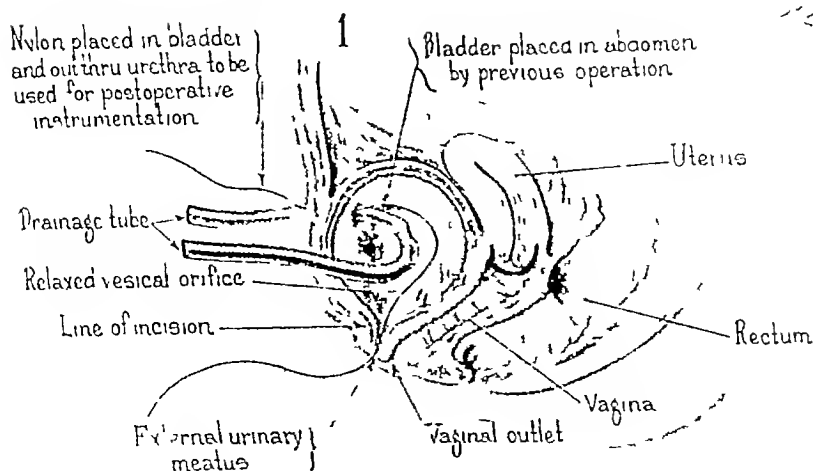
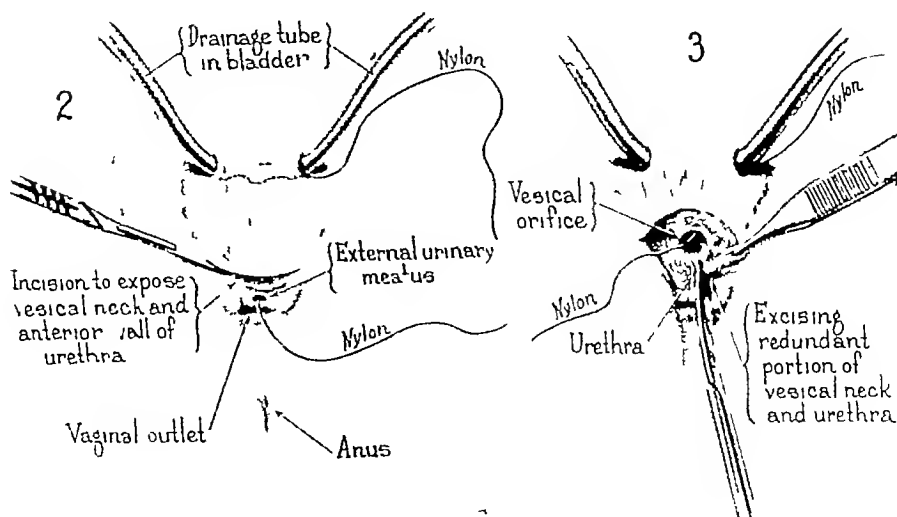


Fig 10 Technique employed to resect urethra previously made and cure in continence. A U shaped suprapubic catheter tube drainage was provided. Urethra was opened and a strip removed on each side, thus leaving very narrow tract from which to form a new urethra (3).



the bladder, is held upward on a clamp. The thread of nylon is seen where it enters the under surface of this flap. In Figure 8, the completion of the operation is shown. In Figure 8, 1, the placing of a subcutaneous stitch of fine catgut to anchor the oval skin flap is shown. In Figure 8, 2, the interrupted sutures of silver wire have been placed to close the wounds.

The patient stood the operation well, the anesthesia was perfect. Convalescence was satisfactory.

August 15, 1940. It is now 6 weeks since operation. The two ends of the U shaped vesical drainage tube emerge

from the openings on each side of the vagina. The wounds have healed *per primam*. A No. 6 F children's sound passes through the new made urethra into the bladder to a distance of about 6 centimeters. A small child's cystoscope also passes without difficulty. The tubes are removed.

August 17. The patient was discharged today. The urine escaped through the openings made for drainage. No urine escaped through the urethra.

The patient returned December 10, 1940. The conditions present are shown in Figure 9. As seen here the exstrophy had not recurred. The abdominal wounds presented a slight keloid effect. The two halves of the clitoris had separated. The urethra was small but incontinent. Examination seemed to indicate that not enough muscle

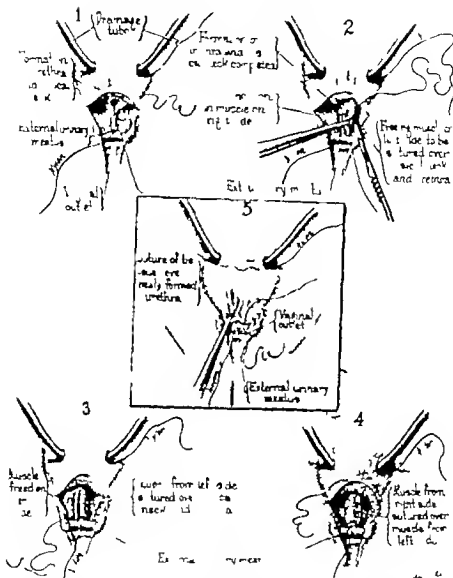


Fig. Urethral closure completed and muscle flaps drawn from each side to cover it, after back skin edges are approximated with silver wire leaving strand of nylon in urethra.

It is given sphincteric control. It is decided to upon the patient again to obtain more and better with which it surrounded the urethra.

On December 20 the second operation was performed. The contracted orifice of the vagina was enlarged by an incision on each side. A goose neck clamp was introduced through the urethra and brought up against the anterior wall of the bladder for a distance of about 7 centimeters from

the urethra. An incision was made through the tissues, skin, and bladder which were held up on its beak, which was then pushed out through the wound. A No. 6 rubber catheter was then drawn into the bladder and out through the urethra. A goose neck clamp was introduced by the side of the catheter and directed against the left antero-lateral wall of the bladder. An incision was made on the left a distance of about 3 centimeters from the

opening which contained the catheter on the opposite side. A clamp passed in the opposite direction through this opening was made to emerge from the urethra where the tube was grasped and drawn back through the opening, as shown in Figure 10, 1 and 2. In this way good drainage was provided for at a distance from the region to be operated upon. In Figure 10, 2, is shown the incision which was made just above the orifice of the previously made urethra. This was enlarged (Fig 10, 3) and after the urethra was opened it was found that too much skin had been used to form the urethra at the previous operation. A strip was excised from each side (Fig 10, 3), thus leaving a very narrow strip of skin (only 3 or 4 mm in width), in the median line posteriorly, and exposing muscle on each side. The technique of closure is shown in Figure 11. In first inset, the greatly resected urethra has been turned in with a continuous subcuticular No 0000 chromic catgut suture on a Dulox needle. This line of suture was continued upward so as to close the bladder opening (Fig 11, 2). It was decided to go at a distance of the median line to free muscle which could be drawn over the new made tight urethra on each side. In Figure 11, 2, the muscle flap, which was obtained on the left side is shown and in Figure 11, 3, the sutures, which were inserted to draw this flap over the new made urethra, are shown. Here also is shown a muscle flap which has been freed by an incision preparatory to covering the first muscle layer. Suturing of this layer of muscle is shown in Figure 11, 4. No 0000 chromic catgut was again employed. As seen here, the newly made tight urethra was covered by two layers of muscle, one drawn from the left, the other from the right. After this it was necessary only to draw down from above the skin flap, which was quite loose and redundant, and to suture the skin and subcutaneous tissue to the adjacent wounds below with fine silver wire. Thus the muscle plastic was completely covered around the very tight urethra which contained only a strand of nylon to be used subsequently as a conductor for the passage of instruments.

Sulfathiazole, 15 grams, three times a day, was given the patient, beginning 2 days before operation and continued. Three days after operation the patient had a skin rash which was diagnosed scarlet fever. The patient was transferred to the isolation ward for 3 weeks. (It seems probable now that this was a sulfathiazole rash and not scarlet fever.)

The catheter, which emerged from the two cystotomy wounds in the upper part of the bladder, worked well, and



Fig 12 Motion picture camera obtained picture of the patient voiding. This is one of the frames. She was able to start and stop the outflow of urine on command and had complete control. Interval between voidings $2\frac{1}{2}$ hours.

no urine escaped through the newly tightened urethra. The sutured wounds healed *per primam* and the double drainage tube was removed on January 12. Two days later filiforms and a No. 14 children's sound were passed through the newly made urethra into the bladder, and a No. 12 urethral catheter was inserted for drainage to facilitate closure of the two suprapubic wounds.

On January 31 the suprapubic wounds having healed, the urethral catheter was removed. The patient voided at intervals through the urethra and with almost perfect control when she left for home on February 6.

For a time leakage occurred from a pin point fistula high up in the skin flap where the strand of nylon emerged. This now has healed, and the patient is voiding naturally through the new made urethra. Urinary control is perfect, the interval from 1 to 2 hours. On July 8 the patient voided about 35 cubic centimeters of urine at a time. She has good control. A motion picture was taken of the child urinating. One of these frames has been enlarged to show this (Fig 12).

July 28. By waking the child at 2 hour intervals at night, voluntary voiding was obtained and bed wetting avoided. The bladder gradually is increasing in size, and the patient is learning to hold urine longer. There is every prospect of a perfect result. She already has good urinary control, voids freely in a small but forcible stream, can stop and start the outflow on order when told to do so. The exstrophy was cured by the first operation, the incontinence by the second.

January 11, 1942 (letter). The patient voids urine at intervals of 3 hours with good control.

This is the story of apparently the first case of exstrophy of the bladder and incontinence that has been cured (B U I 28229). After struggling with these cases for many years, this successful result tempts one to cry, "eureka."

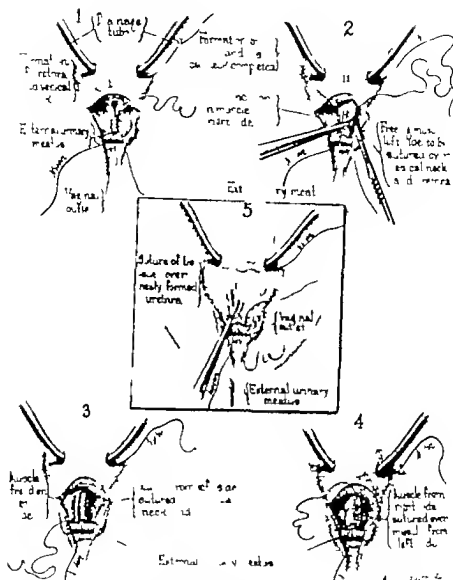


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overs it to give sphincteric control. It was decided to permit upon the patient again to obtain more and better muscle flaps which surrounded the retractor.

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the urethra. An incision was made through the tissues, skin, and bladder which were held up on its beak, which was then pushed out through the wound. A No. 6 rubber catheter was then drawn into the bladder and out through the urethra. A goose neck clamp was introduced by the side of the catheter and directed against the left antero-lateral wall of the bladder. An incision was made on it at a distance of about 1 centimeter from the

opening which contained the catheter on the opposite side. A clamp passed in the opposite direction through this opening was made to emerge from the urethra where the tube was grasped and drawn back through the opening, as shown in Figure 10, 1 and 2. In this way good drainage was provided for at a distance from the region to be operated upon. In Figure 10, 2, is shown the incision which was made just above the orifice of the previously made urethra. This was enlarged (Fig 10, 3) and after the urethra was opened it was found that too much skin had been used to form the urethra at the previous operation. A strip was excised from each side (Fig 10, 3), thus leaving a very narrow strip of skin (only 3 or 4 mm in width), in the median line posteriorly, and exposing muscle on each side. The technique of closure is shown in Figure 11. In first inset, the greatly resected urethra has been turned in with a continuous subcuticular No 0000 chromic catgut suture on a Dulox needle. This line of suture was continued upward so as to close the bladder opening (Fig 11, 2). It was decided to go at a distance of the median line to free muscle which could be drawn over the new made tight urethra on each side. In Figure 11, 2, the muscle flap, which was obtained on the left side is shown and in Figure 11, 3, the sutures, which were inserted to draw this flap over the new made urethra, are shown. Here also is shown a muscle flap which has been freed by an incision preparatory to covering the first muscle layer. Suturing of this layer of muscle is shown in Figure 11, 4. No 0000 chromic catgut was again employed. As seen here, the newly made tight urethra was covered by two layers of muscle, one drawn from the left, the other from the right. After this it was necessary only to draw down from above the skin flap, which was quite loose and redundant, and to suture the skin and subcutaneous tissue to the adjacent wounds below with fine silver wire. Thus the muscle plastic was completely covered around the very tight urethra which contained only a strand of nylon to be used subsequently as a conductor for the passage of instruments.

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SURGICAL AND POSTOPERATIVE TREATMENT OF LARGE VESICOVAGINAL AND RECTOVAGINAL FISTULAS

VIRGIL S. COUNSELLER, M.D. F.A.C.S., Rochester, Minnesota

IT is now nearly 100 years since the classic work of Marion Sims on vesicovaginal fistulas. He contributed more to this subject and brought about greater success in the treatment of the condition than any other person had done prior to 1852. Since then there have been numerous modifications and suggestions as to surgical technique and methods of approach to the fistula. The same is true of fistulas from the bowel to the vagina. The problems involved in the treatment of these fistulas are as difficult as, and are often greater than, the problem of treatment of vesical fistulas. When both vesicovaginal and rectovaginal fistulas exist simultaneously the problems involved in the surgical and postoperative treatment are considerably increased.

It is not my intention to review the various causes of these fistulas, with which all are so familiar. Instead, I wish to point out some of the pitfalls in surgical management which frequently predispose to recurrence of the condition. I also wish to emphasize the importance of meticulous postoperative care for both vesical and rectal fistulas into the vagina, especially those of the larger and more complicated types.

VESICOVAGINAL FISTULA

It is the experience of most surgeons that in about 85 per cent of cases most small vesicovaginal fistulas can be closed at one surgical procedure, especially if previous repeated attempts at closure have not been made. Small vesical fistulas do not often constitute a difficult problem. However, I feel that it should be emphasized seriously that small fistulas such as these occasionally can resist all the skill of an expert surgeon, principally because enough attention has not been given, first, to the situation of the fistula and, second, to residual infection which may be present in the bladder. The importance of the situation of a vesical fistula cannot be too greatly stressed. For example, a small fistula which involves the posterior margin of the internal vesical sphincter is one of the most difficult to close of all fistulas within my experience and it should not be considered

lightly. Since the fistula involves the sphincter the sphincter is, therefore, torn and partially incontinent, resulting from contraction and formation of scar tissue within the circular muscle fibers. It is most difficult to avoid superimposing the vaginal and vesical suture lines at this point without producing distortion of the sphincter and urethra. Apposition of these suture lines predisposes to recurrence. Furthermore, when a catheter is placed through the urethra into the bladder it is almost sure to be in contact with the region of repair and such contact is a very potent factor in recurrence. The catheter always produces irritation and also incites infection which induces breakdown of the suture lines. This factor is one of the chief difficulties in closure of urethral and urethrovaginal fistulas. Urologists who now have become familiar with this fact do not leave a catheter in the male urethra subsequent to surgical repair of urethral fistula or after performance of plastic procedures for hypospadias. The patient is encouraged to arise and micturate in the normal manner or if the surgical procedure has been too extensive a perineal opening is made in the posterior urethra to divert the urinary stream. I am beginning to believe, however, that if a patient can void, the passage of urine over a small repair in the urethra or sphincter is more beneficial than detrimental, since by such a flow all sediment and exudate periodically are lavaged from the suture line. This belief, however, does not apply to fistulas situated entirely within the base or vault of the bladder where they are constantly bathed in urine.

The second factor of residual infection within the bladder in the failure of these small vesicovaginal fistulas to heal is one which is even more serious when large fistulas are encountered, and must be evaluated carefully before operation. A bladder that becomes totally incontinent becomes contracted and infected. Infection in such instances does not produce subjective symptoms, since the irritation cannot induce the desire to void, and the situation becomes annoying to the patient only if the upper part of the urinary tract becomes involved. Irritation and incontinence within the vagina constitute sufficient evidence that the same processes probably prevail within the blad-

der, and the conditions usually are induced by urea-splitting organisms, primarily those of the *Proteus* group, which are the most common and unfortunately the most difficult to eradicate. The formation of incrustations on the mucosa in the region of repair is an extremely potent factor in predisposition of the fistula to recurrence. The factors which are operative in the healing of wounds are exactly the same in this particular situation as they are elsewhere, namely, freedom from infection, proper hemostasis and lack of tension, so that interference with blood supply does not occur.

Large vesicovaginal fistulas of several months' duration constitute the greatest surgical problem from the standpoint of causation, infection and contraction of the bladder, retraction and scarred vaginal and vesical mucosa, involvement of the trigon, ureters, and sphincter. Destruction of the vesical neck, sphincter, and a portion of the urethra often brings about what approaches a hopeless situation in the matter of restoration of vesical function (Fig 1). Such a situation usually is directly attributable to difficult and perhaps faultily performed obstetrical procedures and to the results of radiation therapy for carcinoma of the cervix. In the first instance the earlier surgical repair is undertaken, the greater will be the chances for cure. A patient who has this type of lesion is always entitled to one or two serious attempts at repair, but any further effort is not likely to be successful. The principal effort must be directed, first, toward complete excision of all scar tissue and, second, toward complete mobilization of that portion of the bladder which is involved. This may be a difficult task, since the bladder often appears to be "frozen" against the pubic rami from which it must be entirely separated. The lacerated vesical sphincter retracts exactly as the lacerated rectal sphincter retracts and, therefore, it becomes essential for the surgeon to loosen the fixed residual portion to enable him to reapproximate the circular fibers of the sphincter. Since the trigon usually is almost wholly destroyed, it becomes necessary to narrow the trigon by bringing the ureteral orifices toward the midline. In extensive repairs of this type sufficient vaginal mucosa may not be available for the purpose of complete coverage of the denuded region. If the wall of the bladder will remain closed, the vaginal mucosa will eventually epithelize over the region. Absence of the urethra is not particularly important. If the sphincter can be made to function, so that complete continence results, a urethra can be constructed at a later date, if necessary. Several of my patients have

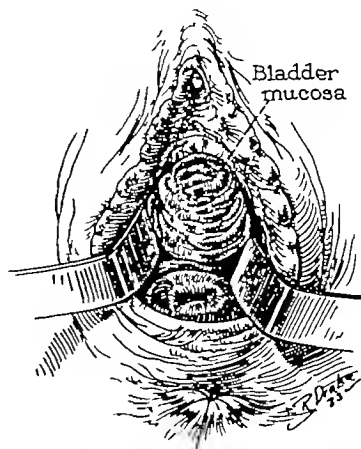


Fig 1 Destruction of the bladder neck, sphincter and portion of the urethra (after Stephenson, G W, and Mason, J C Surg, Gynec & Obst, 1934, 58 1036-1039)

complete urinary control and yet have a very short urethra, they do not have an external urethral sphincter. When reconstruction of the vesical neck is deemed a surgical impossibility, or if failure ensues subsequent to repeated attempts at repair, I think that diversion of the urine to the bowel is the procedure of choice.

A large vesicovaginal fistula which occurs after extensive radium therapy for carcinoma of the cervix is still less likely to be successfully repaired, by virtue of the fact that the tissue at a considerable distance from the edge of the fistula usually is too devitalized to be suitable for repair, and it is often impossible to mobilize this tissue. Any attempt at surgical repair necessarily must be delayed a sufficient length of time to preclude the possibility of local recurrence of the malignant process. Later, when there is no evidence of a residual malignant process, I believe that the patient is best treated by bilateral ureterosigmoidostomy.

Methods of approach. A well planned procedure should be outlined for each patient who has a vesicovaginal fistula. The fistula may be approached vaginally, transvesically, or transperitoneally. Ureterosigmoidostomy also will be considered herein.

Vaginal approach. The result from each of the aforementioned methods may be highly successful, but it is generally agreed now that the method of vaginal approach has many advantages over the others and that the operative risk which accompanies this method is practically nil. During the year 1939, 32 vesicovaginal fistulas were repaired surgically at the clinic, and all were re-

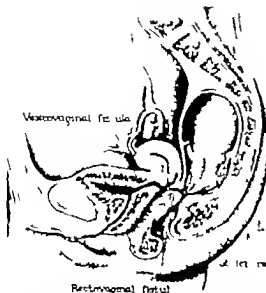


Fig. 2. Illustration of an evaginated and rectovaginal fistula, back as situated high in the vagina (after S. B. Lovelady and J. C. Mason, *Proceedings of the Staff Meetings of the Mayo Clinic*, 935, 49-53).

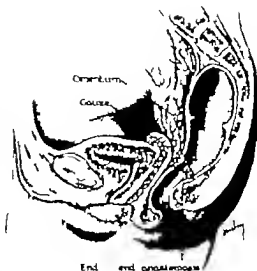


Fig. 3. Performance of hysterectomy and closure of both fistulas from the abdominal side. Portion of the bowel is excised and end to end anastomosis is done. Coarct. draining the cul de sac is in position (after Lovelady and Mason, *loc. cit.*).

paired by the vaginal approach. At the clinic we prefer to have the patient in a modified Krause position with the thighs well separated and the terminal portion of the operating table removed. A Sims speculum is held firmly against the perineum and posterior vaginal wall, which permits easy exposure of the entire wall of the bladder and urethra except perhaps in the nullipara in whom a fistula has occurred subsequent to total hysterectomy. In such an event a Schuchardt's incision is made which converts the vaginal canal into a wide open cavity. The advantages of this approach are obvious. It permits the surgeon to dissect directly on the lesion rather than through dependent cavity as is necessary in the transvesical approach. The ureters can be catheterized with ease, if it is advisable to do so when a faceration has extended laterally to the ureteral orifice. The ramifications of the tear in the wall of the bladder can be more nearly accurately identified. Fistulas that arise after total hysterectomy are most favorably approached in this manner since they are practically always situated high in the vaginal vault and result from passage of suture through the wall of the bladder during closure of the vaginal vault. It is a relatively simple procedure to open the cul-de-sac above the fistulous opening and by placing a finger into the perito-

neal cavity the bladder can be separated from the sac and drawn forward into the vagina.

Transvesical approach. A transvesical approach is desired by many surgeons, perhaps because of a lack of familiarity with the pelvic anatomy, familiarity which is essential. When this method is selected it must be predetermined that the result will be entirely successful otherwise the patient will have both a vesicovaginal fistula and a suprapubic fistula, with a contracted bladder. The problem then, of course, is greater than that which previously existed.

Transperitoneal approach. The transperitoneal approach entails much higher risk than any other method and should be undertaken only in very select cases. A fistula that is situated high in the vaginal vault in an extensively scarred and fixed region (the scarification and fixation usually resulting from postoperative cellulitis) may be more adequately treated by this method. After exposure and closure of the fistula, it is advisable to interpose some fat obtained either from the omentum or from the rectum between the wall of the bladder and the vaginal mucosa. The real danger which may arise when this method is employed is necrosis and leakage of urine, which is always infected, into the peritoneal cavity. It is wise to be prepared for this sequela by splitting

As long as suture material of any type exists within the vagina, there will be a constant flow of exudate, which, if it is not removed daily, will macerate the tissues, an occurrence which will predispose to premature separation of the suture line. For this reason, the vagina is cleansed daily by the careful introduction of a Sims speculum along the rectal wall, to expose the suture line. All mucus, exudate, or blood is removed with a dry cotton sponge and the suture line is painted with a germicidal agent (tincture of merthiolate). This routine also permits the surgeon to observe the healing process.

Specimens of the urine for culture are taken daily directly from the catheter, the bacterial count is estimated, and the acidity is determined. The administration of sulfathiazole is continued during convalescence of the patient. If strict attention is given to this detail, incrustation will not occur on or within the catheter. Prior to institution of this routine at the clinic it was not uncommon for the catheter to become occluded with sediment.

Proper selection of an indwelling catheter contributes much to the comfort of the patient. The catheter employed should be one that does not rest on the trigon or produce pressure against the internal vesical sphincter muscle. To obviate these possibilities, I devised one which consists of a French catheter (male), size 18 or 20, which is introduced through a larger segment of soft rubber tubing about 4 to 6 inches (10 to 15 cm) in length. Approximately 3 to 4 inches (8 to 10 cm) of the soft rubber tube which forms the outer sheath is sectioned to produce four strips of rubber equal in length (Fig 6). The French catheter is held firmly by the remaining segment of the outer soft rubber tube. The catheter is inserted through the urethra for the proper distance and the four strips of rubber are secured to sections of adhesive tape placed toward the pubes and also lateral to the rectum. The patient may move in any position, yet the catheter will remain in the original position, and the exertion of tension on the catheter is prevented.

The patient lies on the Bradford frame for a minimum of 2 weeks, depending on the character of the fistula which she had. After being removed from the frame, the patient remains in bed 2 to 3 days longer. The catheter is then removed and she is instructed to micturate every hour during the next 24 hours, then to micturate every 2 hours for 2 to 3 days, so as gradually to increase vesical function. At the time of dismissal, either the urine should be sterile or bacteriuria should be reduced to grade 1.

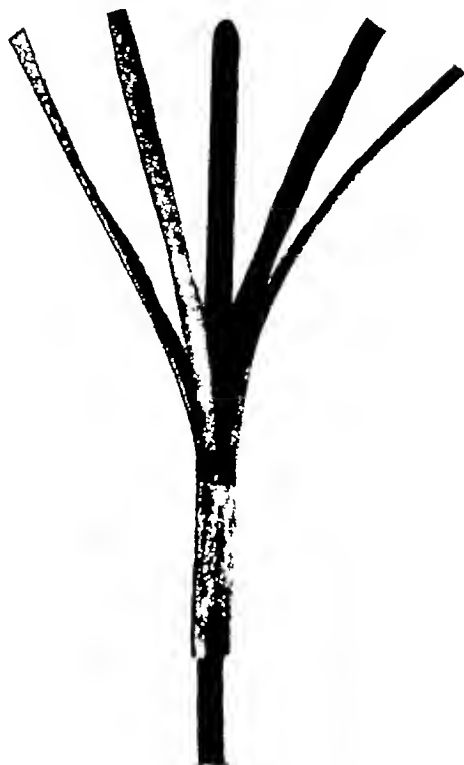


Fig 6 A new method for retention of a nonirritating catheter in the female bladder

RECTOVAGINAL FISTULA

There are three types of rectovaginal fistula which I wish briefly to discuss, namely, (1) that which occurs simultaneously with vesicovaginal fistula, (2) that which develops subsequent to repair of complete laceration of the perineum and (3) that which arises insidiously and in conjunction with an abscess in an anal crypt.

Rectovaginal fistula which develops with vesicovaginal fistula. As a general rule, this type of fistula is situated high in the vaginal wall, as exemplified by the fistula encountered subsequent to radium therapy for cancer of the cervix. This type of fistula occasionally is seen after precipitate labor in a previously nulliparous patient, and, in such instances, complete laceration of the perineum also is likely to have occurred.

Although it may be possible to repair both lesions (that is, vesicovaginal fistula and rectovaginal fistula) simultaneously, the risk of recurrence of either one or the other condition is most certainly considerably greater if such a procedure is carried out. When the vagina has been converted



Fig. 5. Bilateral transplants of the ureters to the sigmoid for carcinoma of the cervix: a, left, 5 minute roentgenogram, in which fairly good concentration is seen on right side and fair concentration is seen on the left side; b, 18

minute roentgenogram, in which good concentration is seen on both sides, ureterectasis, pyelectasis, and calculous grade 2, on the right side and grade 1 on the left side, are present.

monium mandelate in doses of 3 drachms (17 gm). The intake of fluid is restricted to 1000 cubic centimeters in 24 hours. With the gradual decline in numbers of the organisms mentioned, and if the inflammation of the vagina and bladder is receding, surgical repair may be instituted safely, but medication and the making of cultures of the urine must be continued during convalescence of the patient. The advantages of sterile urine in wound healing, in particular during the postoperative course cannot be overestimated.

The appearance of calculi in the upper part of the urinary tract or within the folds of the mucosa of the bladder is a potent cause of continued pyuria while medication is being continued. Surgical repair of large vesicovaginal fistulas is not advisable until all calculi are removed. The advantages of the making of an excretory urogram as a preoperative measure are obvious, for the urogram not only will disclose calculi but will also provide fair index to renal function and will reveal evidence of previous infection in the upper portion of the urinary tract which might become serious complicating factor during convalescence.

Postoperative care. There is no surgical procedure which requires more constant and special postoperative care than repair of a large vesicovaginal fistula. Attention must be directed toward the insuring of continuous flow of urine through the catheter especially after the eighth postoperative day when suture material begins to show evidence of absorption. Should the catheter become occluded or partially extruded, sufficient pressure may accumulate to produce leakage. At the clinic we have attempted to fortify ourselves against occurrence of this accident by adoption of routine in which every patient is placed on Bradford frame in the prone position, about 15 inches or more (5 cm. or more) from the surface of the bed. A two-way irrigating system is provided and the bladder is gently irrigated with few cubic centimeters of solution (boric acid each hour during each 24 hour period. The urine is allowed to drop continually in a basin placed on top of the bed, where it can be observed by both patient and nurse. An effort is made to isolate such patients on one floor where student and special nurses are particularly instructed about nursing care.

nodule will develop on the vaginal wall just behind the perineum, and will remain extremely tender and will finally periodically subside. Subsidence is considered to be due to evacuation of the contents of the abscess into the bowel. The patient appears to be entirely comfortable and free from disease for several weeks, then the nodule recurs on the vaginal side of the wall, with extreme tenderness and discomfort. Finally, the contents of the abscess rupture into the vagina, and fecal material and gas periodically will be discharged through the fistulous opening into the vagina. My reason for drawing attention to this lesion is the fact that attempted closure of this fistula before all the inflammatory process in the rectal wall has subsided will result in surgical failure in 100 per cent of cases. Furthermore, the small focus of infection in the anal crypt usually is only one part of the infectious process and there are ramifications in the form of fistulous tracts in the bowel wall that must be completely excised.

The proper form of attack on such a fistula, then, is a two stage procedure. The first procedure is the problem of the proctologist, and it is usually necessary to cut both sphincter muscles and to destroy completely the perineum. However, this is not true in every instance. When there is evidence that the inflammatory process has subsided and that complete or partial loss of control of the bowel has occurred, the problem becomes that of the gynecological surgeon to reconstruct the anterior rectal wall and the perineum. In other words, the lesion is essentially the same at this particular stage as the lesion which is present at repair for complete laceration of the perineum, after all scar tissue has been completely excised.

Postoperative care Postoperative care of patients who have undergone repair of rectovaginal fistulas is of importance equal to that of postoperative care for patients who have undergone repair of vesicovaginal fistulas. The operative incision must be inspected daily from the vaginal side and from the rectal side. For from 1 to 2 weeks the bowel should be prevented from moving. Exposure of the suture line within the rectum is accomplished by means of a small anoscope. All mucous secretions and flecks of feces should be removed daily through the anoscope, and the suture line within the bowel should be painted with a germicidal agent (merthiolate). A small Sims speculum is placed in the vagina and the anterior vesical and vaginal walls are held firmly to expose

the suture line on the posterior wall. The vagina is cleansed with dry cotton sponges and the suture line is painted with tincture of merthiolate. When the wounds on both the vaginal side and the rectal side of the wall are kept clean, primary union can be expected in approximately all instances. I believe the high incidence of failure in such cases has been due to a disregard of the value of the postoperative care of the wound. The perineum should be kept free of any dressing material whatever, and secretions should be removed from the vagina more frequently than once a day, if necessary. Dry heat should be applied by means of an electric lamp during the day and removed at night.

SUMMARY AND CONCLUSIONS

Attention has been directed to the difficulty of closure of small vesicovaginal fistulas in certain situations with particular regard to the vesical sphincter and ureters.

Sulfanilamide and its derivatives have enhanced the treatment of vesicovaginal fistula in that the drug and its derivatives are able to destroy organisms within the urine in a much shorter period than had been possible formerly and are able thus to maintain the urine in a nearly sterile state during convalescence of the patient. This has been a very great asset in the improvement of end results. Meticulous care must be devoted to the patient during convalescence, to maintain the urine free from infection, to avoid incrustation in the bladder and occlusion of the catheter. The vagina should be cleaned of secretions daily.

Ureterosigmoidostomy has a definite place in the treatment of huge vesicovaginal fistulas in cases in which the bladder has been rendered incapable of again retaining urine.

Rectovaginal fistulas are best treated by complete excision of all scar tissue and re-establishment of the normal character of the rectal tube. Particular attention is directed toward those small fistulas which originate in an anal crypt, a circumstance in which it is essential that the surgeon understand the etiology of the condition and the clinical course of the patient. Postoperative care is similar to that for patients who have undergone repair of vesicovaginal fistulas in that suture lines in both the rectum and vagina must be kept clean daily. This can be done by the use of a Sims speculum, a small anoscope and dry cotton swabs. Attention to these details will greatly improve the number of instances of primary healing.

A FUNDAMENTAL ERROR IN CURRENT METHODS OF INGUINAL HERNIORRHAPHY

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COMMONLY in the experience of the dissector and of the surgeon, structural features are encountered in surgically important areas of the body which are inadequately described in the textbooks upon which they have been dependent. In recent studies (McVay and Anson, 1940) the authors have found, for example, that the available accounts of the aponeurotic and fascial continuities from the lower abdomen into the thigh are highly conventionalized and scarcely satisfactory for the guidance of the critical surgeon. Certain of the features encountered in the study explain the frequency of recurrence, while others suggest the desirability for modification of the usual methods employed in inguinal herniorrhaphy.

The current brief report will review the salient features of inguino-femoral anatomy and describe an operation based upon this morphological study. Although brief it is hoped that this preliminary report will, by stimulating others, accelerate the accumulation of statistical data on similar cases, and will be of aid to those who have requested detailed information on the technique involved.

ANATOMY

External oblique. In the inguinal part of the abdominal wall, the external oblique is an aponeurotic plate covered on each surface by an investing fascial layer. It is, however, not a complete aponeurotic plate since it is defective at the triangular hiatus (loosely termed the subcutaneous inguinal "ring") and in an area, lenticular in outline, caudal to the inguinal ligament (Fig. 1). In

From the Department of Surgery, University Hospital, Ann Arbor, Michigan, and the Department of Anatomy, Northwestern University Medical School, Chicago, Illinois (contribution no. 345 from the latter). The anatomical aspect of the present report represents a brief consideration of earlier observations by the same authors (34, 35, 36, 37).

The anatomical investigation, as presented at Northwestern University Medical School by the authors, in collaboration, the technical procedure, as directed by Dr. C. B. McVay, during the progress of the laboratory study and put into service at the University of Michigan with the assistance and co-operation of Dr. F. A. Collier, professor of surgery in the latter institution (38).

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these areas, which are largely devoid of aponeurotic fibers, anatomical closure is effected by the fasciae which fuse back-to-back as they stretch across each opening. Between the crura of the "ring" they are carried downward into the scrotum as the external spermatic fascia; below the inguinal ligament they are continued inferiorly as a superficial component of the fascia lata.

Therefore, so far as the outermost of the three abdominal layers is concerned, it may be said that the barrier to herniation is incomplete in the presence of a patent processus vaginalis; the descending intestine or omentum need only enlarge the hiatus between aponeurotic crura and dilate the surrounding fascial envelope. Since the fasciae serve to bind together adjacent aponeurotic bands so that totally they form a plate under stretching in herniorrhaphy, may so weaken the covering fibrous layers that the way is paved for a recurrence when adjacent aponeurotic bands are drawn apart, shortened by suturing, a new hernia may occur through a cleft artificially produced either in the aponeurosis itself or distal thereto in the area of weakness between inguinal and femoral regions.

Internal oblique. Whereas the external oblique is chiefly aponeurotic in the inguinal region, the corresponding part of the internal oblique usually contains some muscle fibers, especially in its lateral portion (Fig. 2). In the inferomedial portion of the greater number of specimens, however, aponeurotic fibers diminish in size and number and muscle fascicles become sparse. The investing fascial layers then remain as the sole representatives of the internal oblique. On the spermatic cord, too, fascicles are few so that this intermediate one of the funicular coats is very similar to that derived from the conjoined muscle fasciae of the external oblique.

The lower portion of the internal oblique—that is, its cremasteric portion—arises from the ilio-psoas fascia as the latter lessens the pelt is for the lower extremity. Its attachment to the inguinal ligament is by means of a rather delicate tissue. It is unlike the other funicular coats in that the proximal (abdominal) orifice of the tube which it

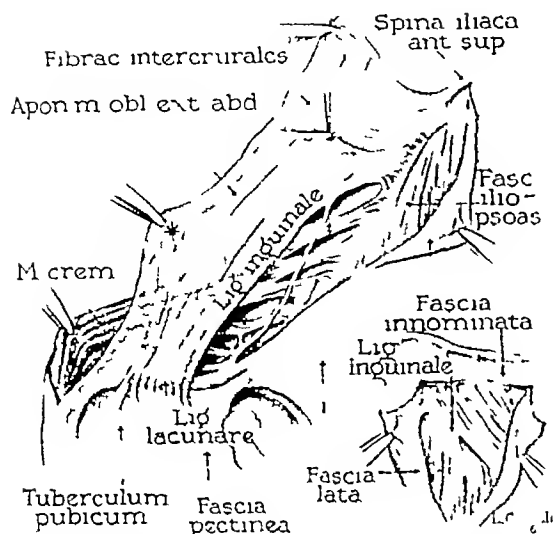


Fig 1 The external oblique aponeurosis freed of its external layer of fascia, showing that the inguinal ligament itself is a marginal structure, separate from the fascia lata of the thigh and independent of cremasteric part of internal oblique. Inset shows fascial continuities, opposite side.

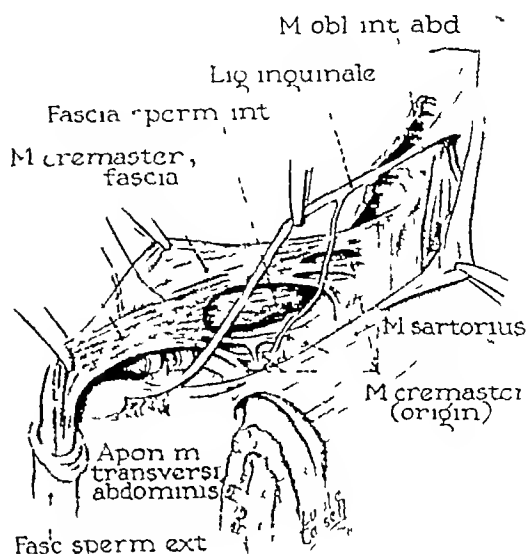


Fig 2 The internal oblique is exposed by removal of all of the external oblique except its lowermost aponeurotic fibers (inguinal ligament), the former layer, in its cremasteric (funicular) part is partially fascial, it arises from the ilio-ipoas fascia, not from the inguinal ligament.

forms is an elongate oval in outline, not a circle (opened in Fig 3), it does not completely surround the cord until that structure emerges through the subcutaneous inguinal ring. It is, therefore, a poor barricade, being capacious at its beginning and chiefly fascial through the greater part of its length.

Transversus abdominis The inguinal portion of the transversus abdominis muscle is more aponeurotic than it is muscular (Figs 3 and 4), its lowermost part arises from the ilio-ipoas fascial tube as does the cremasteric portion of the internal oblique. The insertion of this lowermost portion of the transversus is not to the inguinal ligament as one might conclude from present methods of herniorrhaphy but to Cooper's ligament on the superior pubic ramus.

Almost without exception that part which is carried downward upon the cord is purely fascial (as its name, internal spermatic fascia, would indicate). Similar to the funicular sheath is the femoral sheath, for this, the fascial layers of the transversus fuse to form the anterior component of a tubular prolongation (Fig 4 and inset), the ilio-ipoas fascia forms the posterior component. The inner fascial contribution from the transversus layer is the transversalis fascia but the outer bears no special name. The femoral differs from the funicular sheath in transmitting vessels

chiefly, in hernial cases it resembles the aforementioned sheath in containing (in its medial compartment) a peritoneal diverticulum.

SURGERY

All the recognized methods of inguinal herniorrhaphy which have been devised since the publication of the works of Bassini and Halsted, are alike in one respect: in each of them the various inguinal layers are sutured to the inguinal ligament. Although minor variations are legion, they seem to possess this feature in common.

The current article is entirely in agreement with those stating that simple excision of the hernial sac is adequate in a small indirect inguinal hernia when the abdominal inguinal ring is not markedly dilated, in this type of hernia, if no weakness of the posterior wall is demonstrable, passing sutures through the so called conjoint tendon and fastening it to the inguinal ligament will serve only to weaken layers and to reduce the defenses against a direct inguinal hernia. A large indirect hernia and a direct inguinal hernia present the same problems for repair. In the former, the medial extension of the dilated abdominal inguinal ring may lie next to the rectus muscle, with the result that the entire posterior wall of the inguinal canal (including the area of Hesselbach's triangle) is attenuated and the bulk of its tissue displaced medialward.

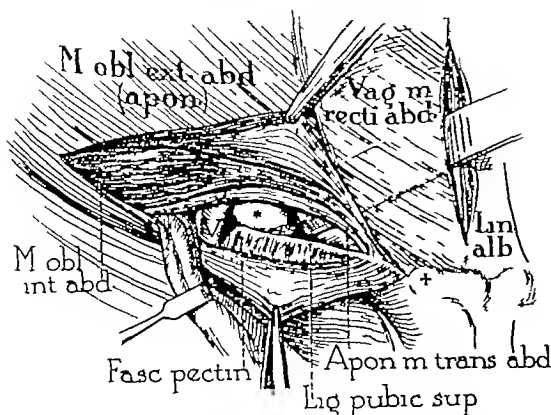


Fig 5 Dissection demonstrating the stage in a direct inguinal herniorrhaphy in which the hernial sac has been excised. The relationship of the inguinal ligament, Cooper's ligament, and the margins of the transversus and internal oblique aponeurosis is demonstrated. The margins of the latter are sharp because the attenuated portions have been excised.

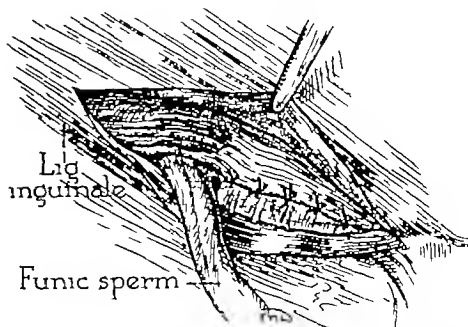


Fig 6 Herniorrhaphy, showing the aponeurotic lower margins of the transversus and internal oblique sutured to Cooper's ligament.

dominis aponeurosis were not readily available, then there might be some reason for using the inguinal ligament, but, actually, the layers themselves and the heavy band into which they insert medially are conveniently situated for surgical use, the latter band, termed the superior pubic, or Cooper's ligament is a dense fibrous structure lying on the anterosuperior aspect of the superior pubic ramus from the pubic tubercle medially to the vicinity of the femoral vein laterally (Fig 5). It is composed of fibers from the transversus aponeurosis and attached transversalis fascia, a lateral expansion of the rectus tendon of insertion and the pectineus fascia. Cooper's ligament is used rather consistently in the repair of femoral hernias, usually, however, the inguinal ligament as well as the transversus aponeurosis and internal oblique aponeurosis are sutured to it, as described by Moschowitz. Dickson, however, advocated merely suturing the transversalis fascia to Cooper's ligament in the repair of a femoral hernia, ignoring the inguinal ligament. The first inguinal herniorrhaphy method known to these authors that utilized Cooper's ligament, is that described by Babcock. This method, however, uses only the medial portion of Cooper's ligament in the immediate vicinity of the pubic tubercle. Robins has subsequently advocated suturing to Cooper's ligament after the method of Babcock, and J. R. Veal and D. D. Baker utilize the superior pubic ramus in their periosteal graft.

The operation suggested is in essence a restoration of the normal inguinal anatomy. The incision

of the skin and method of ligating the hernial sac are in no way different from those in general use, the principle of high ligation and of utilizing fascial or aponeurotic structures is adhered to, the suggested method differs from others in that it ignores the inguinal ligament. After the sac is removed or imbricated, as the case may be, the superior pubic (Cooper's) ligament is isolated, and freed of adjacent preperitoneal connective tissue (Fig 5). If anomalous obturator vessels are to be ligated and severed, the small artery to the pyramidalis muscle, sometimes encountered, should also be ligated. The inferior margin of the transversus abdominis aponeurosis and attached transversalis fascia is clarified by excising any attenuated portion secondary to the hernia and freeing it from the underlying preperitoneal connective tissue (Fig 5). This aponeurosis is then sutured to Cooper's ligament from pubic tubercle to the femoral vein by a series of interrupted silk sutures (Fig 6). If the lower border of the internal oblique is aponeurotic, its substance is to be included in the sutures. If closure cannot be accomplished without undue tension, relaxation is accomplished after the method of Falis. This type of closure leaves a small defect between the abdominal inguinal ring and femoral vein (Fig 6), normal anatomy is here restored by suturing the transversalis fascia to the anterior surface of the femoral sheath. It is worthy of special comment that, if the transversus abdominis aponeurosis is sutured to Cooper's ligament as far laterally as the femoral vein, the femoral ring is obliterated, by this means the possibility of a femoral hernia is obviated.¹

It will be noted that after the suturing of the transversus aponeurosis to the ligament of Cooper

¹The important relationships of the lacunar ligament, Cooper's ligament, femoral ring, transversus abdominis aponeurosis and falx inguinalis have been discussed in the earlier article by the present authors (McVay and Anson, 1940). Suffice it to say that the standard descriptions of these structures and their mutual relationships are not accurate.

and the establishment of the continuity of the transversalis fascia to the anterior femoral sheath that a pyramidal space is produced. The cord is dropped into this and the external oblique aponeurosis is closed over it so that the spermatic cord emerges at the site of the subcutaneous inguinal ring. The obliquity of the inguinal canal is simultaneously restored. It should be acknowledged that the suturing of the layers to Cooper's ligament is technically more difficult because of the latter's deep position. There is also danger of injuring the femoral vein. A simple precaution forestalls such an accident by the use of a vein retractor or the index finger for protection of the femoral vein, and a small ribbon retractor to keep the preperitoneal connective tissue out of the field, adequate exposure is obtained.

SUMMARY

In the repair of large indirect and direct inguinal hernias, it is recommended that the inguinal layers be sutured to Cooper's ligament and not to the inguinal ligament. It is pointed out that the inguinal strata are not a suitable substitute for such attachment on the contrary, the superior pubic ligament, Cooper's ligament, which is the normal insertion, is readily accessible intrinsically strong and directly fixed to bone.

For those who would seek critical use of anatomical illustrations the following additional descriptions may be of service. In Figure 1, the deep (transversalis) fascia on the inner surface of the external oblique aponeurosis, with its contained spermatic fibers, has been unrolled except in quadrilateral areas near the anterior superior iliac spine. The femoral layer and the proximal part of the fascia lata have been reflected inferiorly to demonstrate their continuity at the groin, and to expose the unattached central portion of the inguinal ligament. Through the latter the cremaster fascicles are exposed. They arise from the iliopectineal fascia and the lat-

er, medial femoral vein, the deep layer of the fascia lata. The medial femoral vein is attached to the iliopectineal fascia. In the inset in Figure 1, the deep fascia over the inguinal ligament has been split apart, but has been drawn aside to demonstrate its continuity of the fascia lata with the transversalis fascia (opposite half of body). The spermatic cord of the external oblique continues with the iliopectineal fascia. Inset in Figure 1, the spermatic cord is exposed. The external oblique aponeurosis is reflected to reveal the external oblique aponeurosis. The external iliopectineal fascia has been reflected downward on the spermatic cord, thus exposing the cremaster layer. The inguinal ligament, contained in the iliopectineal fascia, has an attachment to the pubic tubercle. The external oblique muscle has been reflected near the arch of its muscle fibers from the iliopectineal fascia and the lateral femoral circumflex artery. The cremaster layer, attached to the inguinal ligament, contains the spermatic cord. The cremaster layer, visible in the inset, is a source of cremaster fibers (which the latter are fixed of their spermatic fascia). A retractor, placed deep to the cord and the cremaster elevates the preperitoneal connective tissue to expose attachment to the pubic process, the continuity between the spermatic cord and the femoral sheath demonstrated in Figure 1. The cremaster layer, including the superior crus, has been divided along the cord to demonstrate in part the medial portion, entirely femoral. The cremaster extends inferiorly deep to the femoral ligament, so as to arise from the femoral vein, above the spermatic cord. Clearly, in Figure 1, the proximal stump of the spermatic cord has been elevated to show the external appearance of the abdominal inguinal ring, the external spermatic foramen has been rolled backward, leaving the contents of the cord in their preperitoneal connective tissue (covered by the femoral). The cremaster muscle remains in two sets of fascicles arising from the iliopectineal fascia. The inguinal ligament remains in medial and lateral chords. The superior crus of the femoral vein has been cut, only the stump of an attachment remaining, the femoral vein has been turned inferiorly to place the femoral vein from iliopectineal fascia (transversalis abdominalis) into femoral sheath. The separation of the femoral vein from the portion of the pubis (at 2) is shown in Figure 1, the femoral sheath, unrolled, shows its continuity with the iliopectineal fascia and of its continuity with the preperitoneal connective tissue.

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BASILAR INVAGINATION OF THE SKULL— SO CALLED PLATYBASIA

Report of Three Cases in Which Operation Was Done

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FREQUENTLY the stimulus of presentation of observations at one of our meetings results in subsequent reports of similar clinical observations. Three years ago when Chamberlain reported his cases of so called platybasia most of us realized that we had probably overlooked the surgical possibilities in this condition. Now that we are aware that "platybasia," or more nearly accurately, basilar invagination of the skull, is a deformity of the occipital bone, which narrows the foramen magnum, and of the upper cervical vertebrae, which flattens the spinal canal and that removal of the bone which is compressing the underlying brain and spinal cord usually will be followed by relief of symptoms, the syndrome is receiving more recognition.

The term "platybasia" in recent years unfortunately has been applied to a condition which is more properly described as 'basilar invagination of the skull,' or "basilar impression." According to anthropologists, true platybasia denotes an abnormal obtuseness of the sphenoid angle which results in a flattening of the basal, or as it is often termed, the sphenoid angle. The normal sphenoid angle is that angle which is situated between the line from the foremost point of the foramen magnum to the center of the sella turcica and from this point to the root of the nose. The angle varies normally from 115 to 150 degrees. The condition of basilar invagination of the skull has been known to anthropologists and pathologists for many years, and basically, the condition represents a developmental anomaly of the occipital bone and upper part of the cervical region of the spinal column.

According to Schueller, who described the roentgenographic features of the condition in 1905, basilar invagination is designated as an unusual change in the base of the skull, the most striking feature of which is the upward bulging of the posterior cranial fossa around the foramen

magnum. When viewed from inside the cranial cavity the base of the skull in cases in which the condition is typical exhibits an elevation of the edge of the foramen magnum lying between the pyramids of the temporal bones. The clivus in the presence of basilar invagination forms a convex bend, the vertex of which comes to lie at the level of the floor of the sella turcica so that the so called basilar or sphenoid angle approaches a straight angle and not an obtuse angle, as in true platybasia, which is not associated with neurologic symptoms. The elevated portions of the occiput are considerably thinned, and the condyloid processes are more or less rudimentary. According to Schueller, in the classic case also are exhibited congenital variations of the upper cervical vertebrae. The first cervical vertebra is rudimentary in type and the posterior arch is usually fused to the lower surface of the occipital bone bounding the foramen magnum. The spinous process of the second cervical vertebra is fused with that of the third cervical vertebra.

In 1934 Ebenius described 4 cases of basilar impression (platybasia or basilar invagination) in which neurological changes were associated. Suboccipital decompression was carried out in 3 cases in an effort to relieve the symptoms. In 1938 Chamberlain described 4 cases of basilar impression (platybasia), in 2 of which suboccipital decompression had been carried out for the relief of symptoms. As a result of Chamberlain's report, interest in the condition was stimulated in this country. Although the abnormality is more properly designated as "basilar invagination," the term "platybasia" has become popular through Chamberlain's reference to it. Chamberlain has called attention to the fact that in lateral roentgenograms of the normal skull the shadows of the atlas and odontoid process will lie caudad to a line connecting the posterior edge of the hard palate and the posterior margin of the foramen magnum (Chamberlain's line).

Secondary basilar invagination may develop in the presence of any systemic skeletal disease in which the calvarium is softened, Paget's disease,

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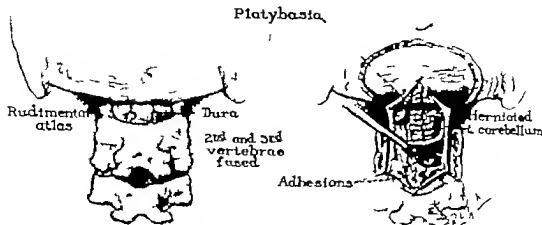


Fig. Basilar invagination, showing the condition found at operation before and after the bone was removed and the dura opened.

hyperparathyroidism, osteomalacia, and the like.

Gustafson and Oldberg reported several cases, with operative or necropsy confirmation, in which a syringomyelic picture of dissociated sensory loss was found on sensory examination of the patients. In our cases careful sensory examination failed to disclose any sensory changes except disturbance in the sense of pain occurring twice in the right side of the face. It is important to recall that the clinical picture may apparently vary somewhat from patient to patient. The stage of development at which the patient is seen may also prove confusing. We have recently seen at the clinic several patients who presented the classic roentgenologic picture of basilar invagination of the skull but who had, so far as could be found, no symptoms or signs indicative of disease of the nervous system. Whether or not these will occur at some later date remains to be seen.

It is an accepted fact that several skeletal anomalies may afflict a single patient who has basilar invagination of the skull, a fact which suggests that this condition usually rests on a congenital or developmental basis. List has comprehensively described anomalies of the occipital bone, atlas, and axis. Among the more prominent of these may be mentioned the Klippel-Feil deformity or fusion of two or more cervical vertebrae, the Arnold-Chiari deformity, or lengthening of the pons and medulla oblongata with herniation of the cerebellum into the spinal canal, spina bifida occulta, or failure of fusion of the laminae of one or more vertebrae and syringomyelia, or the existence of cavitation within the substance of the spinal cord, the caudal often being sur-

rounded by a zone of gliosis. Gustafson and Oldberg emphasized the almost invariable occurrence of adhesions about the brain stem and cerebellum in the portion that has herniated through the foramen magnum. They stated that operation which consists in enlargement of the foramen magnum without opening of the dura and freeing of these adhesions is not productive of relief and judging from our observations at operation, we concur in this opinion. It is possible that the late onset of symptoms among patients who have basilar invagination of the skull, although the skeletal deformities probably are present during most, if not all, of the patient's life, may be explained by the fact that symptoms might not occur until these adhesions form. The treatment of basilar invagination which produces symptoms is purely operative and in the reported cases has been productive of good results if the operation was not deferred too long.

REPORT OF CASES

CASE 1. The patient is a man aged 46 years, by occupation clerk. Except for renal colic from which he had suffered years prior to his coming to the clinic and the occasional finding of albuminuria of an undetermined cause, the patient's history is not remarkable. About 22 months previous to the time of examination, marked occasional mild diplopia, and slight wastage of gait had developed. These symptoms had been completely relieved by ocular refraction and prescription of new lenses for his glasses. Eight months previous to the examination, however, definite and persistent wastage of gait, which was worse in the dark, appeared and persisted. During the previous 5 months he had noted an occasional throbbing type of paresthesia of the right hand and arm. He had had enough sometimes caused his legs, and occasionally his arms, to feel momentarily very weak. Frontal and occipital head

ache, which was worse on his arising in the morning, had become more frequent. For 2 months prior to his visit to the clinic slight difficulty in the swallowing of liquids had been noted.

The patient registered at the Mayo Clinic on November 9, 1940. Results of general medical and laboratory examinations were negative, as were results of careful examination of the ocular fundi. Neurological examinations disclosed coarse nystagmus on lateral gaze in either direction. The left side of the face, including the forehead, was slightly but definitely weak. Hypesthesia to pain was present on the right side of the nose and adjacent portions of the right part of the forehead, right cheek, and upper lip. The right corneal reflex was slightly diminished. The left side of the tongue was moderately weak and definitely atrophied. The gait was markedly ataxic, but inco-ordination of the arms or legs, and adiadococinesis or the rebound phenomenon were not present. Thus, to recapitulate, there was evidence of involvement of the midline cerebellar structures (flocculonodular lobe) and of the right fifth cranial nerve nucleus (nucleus of the descending tract of the trigeminal nerve) and of the left seventh and twelfth cranial nerves. The differential diagnosis included tumor of the brain stem, or in the midline of the cerebellum, and a vascular or degenerative lesion of the brain stem and basilar invagination of the skull. The characteristic roentgenological observations consisted of true invagination of the base of the skull in the region of the posterior cranial fossa, plus anteroposterior narrowing of the foramen magnum with congenital variation of the first three cervical vertebrae. The posterior portion of the first cervical vertebra was fused to the inferior portion of the skull, and the second and third cervical vertebrae were fused both in the body and in the posterior portions.

The pressure on the pons and medulla oblongata, caused by a narrowed anteroposterior diameter of the foramen magnum and upper cervical vertebral canal, being responsible for the symptoms, the surgical procedure indicated was that of removal of the posterior arch of the foramen magnum and spinous processes and laminae of the upper cervical vertebra.

With the patient in the upright position and under the influence of intratracheal anesthesia, a midline incision was made over the suboccipital and upper cervical regions. This incision was carried down through the skin and muscles to the suboccipital bone and the spinous processes of the cervical vertebra. The muscle and periosteum were separated from the bone of the skull, and subperiosteal dissection was carried out about the spinous processes and laminae of the upper cervical vertebra. As the dissection proceeded we could see that the arch of the atlas was absent and that the second and third cervical vertebrae were fused, as was apparent in the roentgenogram. Laminectomy was done, and the fused spinous processes and laminae of the second and third cervical vertebrae were removed. We then were able to remove the posterior arch of the foramen magnum with double rongeurs, and a modified type of suboccipital craniotomy was done. After this the dura was opened and the inferior tonsil of the right cerebellar lobe was seen to have herniated through the foramen magnum to the level of the third cervical vertebra. Definite compression was present, indicative of a narrowed foramen magnum, and adhesions existed between the meninges, the pons and cerebellum. These adhesions were divided and the cerebellar lobe was gently dissected free from the underlying structures. Some definitely anomalous vessels situated around the cerebellar tonsil prevented amputation of the tonsil, which procedure has been suggested in cases in which the condition is extreme, as it was in this one. The entire region appeared to have been compressed, but after

the adhesions had been divided and the inferior cerebellar tonsil had been dissected free, much more room was provided, and definite decompression was accomplished (Fig. 1). The dura was then closed with interrupted silk sutures and the incision was closed with interrupted catgut in the muscle and silk in the skin.

In the preceding case the condition was so typical from the diagnostic and surgical standpoints that it really seemed that there was no question that surgical intervention was a safe and logical procedure. However, in the next case, compression was so great that respiratory difficulties were encountered throughout operation, and it was necessary to leave the dura open in order to obtain the maximal amount of relief.

CASE 2. A boy 16 years old was brought to the clinic on March 3, 1941, complaining of difficulty in swallowing liquids, a difficulty that had been present for $1\frac{1}{2}$ to 1 $\frac{3}{4}$ years prior to the time of his visit. Solid food could be taken without any difficulty. During the 2 years prior to the time of his visit he had suffered from some degree of weakness and loss of weight. He had always had some limitation of lateral motion of the neck, without pain.

Aside from osteomyelitis of the right femur, which had developed in 1934 and had taken a year to heal, the patient had remained in good health until about 1938, when he had begun to experience frequent attacks of stiffness and soreness in his neck. A violent cough or sneeze invariably would produce pain in nape of neck, more on the left than right, with extension of the pain up over occiput. Lying down would relieve this distress within a few minutes.

Nothing more of significance was noted until about March, 1939, when he had begun to experience difficulty in swallowing liquids. He would choke on liquids and had trouble with phlegm in his throat in the mornings. During latter half of 1939, he had begun to notice difficulty in walking and marked clumsiness developed in use of his hands. These symptoms had been progressive.

Shortly before the patient was admitted the father had noticed that while the boy was sleeping, he breathed in an unusual manner. Respirations which were shallow and frequent were followed by about three deep breaths taken slowly, followed in turn by a period of apnea which lasted for as long as 30 seconds. Then the process was repeated.

During the last 2 years prior to his visit, the patient had increased in height at least 12 inches (30 cm.).

The essential observations included a cerebellar type of ataxia, which was more marked on the left side, and elicitation of Romberg's sign. The patellar and achilles reflexes were increased and Babinski's, Chaddock's and Rossolimo's signs were elicited bilaterally. Rapid horizontal nystagmus was marked on the patient's looking toward either side, with slight nystagmus on his looking upward. Vibratory sense was moderately decreased at both external malleoli. The muscles of both upper extremities were definitely weak, but the strength in the lower extremities seemed normal.

Roentgenological examination of the cervical part of the spinal column and the skull revealed a congenital anomaly of the upper part of the cervical region of the spinal column, with a well defined basilar invagination deformity. There was an anomalous deviation of the body of the second cervical vertebra with resultant deformity of the odontoid process and anterior portion of the first cervical vertebra, there was also spina bifida occulta of the sixth and seventh cervical vertebrae. The lateral view of the skull and upper

part of the cervical region of the spinal column revealed deformity of the foramen magnum and first cervical vertebra, typical of basilar invagination.

The patient was operated on on March 8, 1941 at which time suboccipital decompression and laminectomy in the upper part of the cervical region was done. Because of the respiratory symptoms when the patient was asleep it was thought best to attempt to carry out the operation with the patient under the influence of intratracheal anesthesia. Induction of anesthesia was begun by the intravenous administration of pentothal sodium, when the patient's respiration ceased. Under artificial respiration he began to breathe normally and regional anesthesia was used thereafter throughout. With the patient in the upright position through midline incision, the arches of the first, second, and third cervical vertebrae are removed. The second and third are fused and there is definite projection of the left side of the laminae which were compressing the medulla oblongata. Suboccipital craniotomy consisted of removal of the arch of the foramen magnum and the adjacent bone, for about 4 centimeters. At about this time the patient's breathing became very labored and he became comatose. He quickly opened the dura and found marked herniation of both cerebellar lobes to the level of the third cervical vertebra. Adhesions between the meninges, medulla oblongata, and the brain stem were present; these were rapidly divided. When attempted to close the dura compression of the underlying part of the brain occurred. For that reason the dura was left open. Carbolic incision was used for closure of the opening, and the muscles were closed by the usual manner.

After this operation the patient recovered completely and was allowed to return to his home. There was marked absence of nocturnal dyspnea, and the patient's general condition was greatly improved. In letters written after the operation it was stated that he was greatly relieved of all symptoms, was awakening normally and was sitting and sleeping without change in respiratory rate.

In the third case, the patient, although incapacitated for work, did not have a classical syndrome, although the roentgenograms of the head were typical. At operation the typical flat foramen magnum was found, with basilar invagination of the skull, but there were no anomalies of the cervical vertebrae and little herniation of the cerebellar lobes. The postoperative improvement, although it was subjective, indicated that operation was justified.

CASE 3. A male, aged 5 years, was admitted to the clinic on April 1941, complaining of numbness and weakness of the legs which had occurred intermittently during the previous 6 months. In October, 1940, the patient had noticed some numbness as he arose from the supine position. This had been associated with increased bilateral "tiredness" of his legs. A sensation described as "electric pins and needles" had seemed to affect the front of his feet and legs to his knees on his climbing the stairs. By November, 1940, this condition had progressed to such point that it was necessary for him to quit his work. His legs had continued to become weaker particularly about the knees. In February 1941 he had noted the same sensation in his arms as had been present in his legs, associated with numbness in the upper part of

the thoracic region of the spinal column. This had been intermittent. During the 3 months prior to his coming to the clinic he had noted paresthesia involving both lower extremities, but more on the right side. For 4 or 5 months he had experienced intermittent attacks of weakness that had favored the right side of his head.

On examination bilateral increase of patellar reflexes and static tremor on the left were found. Definite spasmus was detected on lateral gaze. Roentgenological examination of the skull revealed flattening of the foramen magnum and typical basilar invagination of the skull. The spinal fluid was under normal pressure. Spontaneous block was not present, and the content of protein was normal. There were, however, slow increase and rapid decrease in the pressure of the spinal fluid on and after performance of the Queckenstedt or jugular compression test.

On April 2, 1941 with the patient in the upright position and under intratracheal anesthesia, midline incision was made over the occipital and upper cervical regions. Fusion of the upper cervical vertebrae was not present, and when the arch of the foramen magnum was removed the dura was opened. Although herniation of the cerebellar lobes was not so marked as in previous cases, definite adhesions were situated between the meninges and the inferior poles of the cerebellar lobes. After an uneventful convalescence the patient returned to his home.

SUMMARY

Three patients with roentgenographic picture of basilar invagination of the skull are reported. In 2 of the cases associated anomalies of the upper cervical vertebrae also were present. Clinical symptoms suggested involvement of the spinal cord in the upper cervical region and the brain stem in all 3 cases, whereas neurological signs indicated a lesion of the cerebellum or its tracts in all cases, and in one case each, a lesion of the brain stem, and a lesion of the spinal cord in the upper cervical region. Marked respiratory difficulty occurred in one case.

Operation was carried out in each case, and adhesions between the meninges and inferior poles of the cerebellar lobes and brain stem were present and were freed in all cases. In 2 cases marked herniation of portions of the cerebellar lobes occurred. Relief from symptoms was striking in all cases.

The characteristic roentgenographic picture of basilar invagination of the skull has been encountered among several patients who had neither the clinical symptoms or signs of involvement of the nervous system.

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AN EXTRA-ARTICULAR OPERATION FOR RECURRENT DISLOCATION OF THE SHOULDER JOINT

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FOR the treatment of habitual dislocation of the shoulder the writer introduces a simple and improved method which is accomplished by an attack that intends to be extra-articular throughout¹ The technique to be described was developed to replace the longer and more complicated procedures employed today, in which articular exposure, excessive manipulation and injury to synovial lining and capsule are objectionable features

Nicola, in considering the pathology underlying recurrent dislocation of the shoulder, listed three main groups (1) bony, (2) capsular, and (3) muscular

"1 In the bony group are included (a) Defects in the head of the humerus, either congenital or acquired after the first dislocation Atrophy of the head of the humerus, infantile paralysis, or congenital defects (b) Defects in the glenoid cavity, consisting of acquired fracture of the edge, or shallowness of a congenital type (c) Fracture of the greater or lesser tuberosities of the humerus

"2 In the capsular group are included (a) Detachment of the joint capsule from the anterior or inferior margins of the glenoid fossa (b) Enlargement of the joint capsule from relaxation following repeated tears

"3 In the muscular group are included (a) Weakness of the supraspinatus and infraspinatus muscles (b) Contracted pectoralis major, teres minor, and latissimus dorsi"

According to Steindler and others, the principal pathological feature in habitual dislocation of the shoulder is the relaxation of the antero-inferior capsular apparatus The original rent in the capsule is filled in by fibrous tissue and the resulting redundancy predisposes to subsequent dislocations, which occur on abduction and outward rotation of the arm, in many instances during epileptic seizures On the other hand, Bankart believes that the underlying pathology in traumatic dislocation of the shoulder joint occurs

¹The technique herein described was developed and perfected in the Department of Anatomy of the University of Illinois, College of Medicine, with the aid of Dr Otto F Kampmeier Professor of Anatomy and Head of the Department. The writer also wishes to thank Dr Jack Kirschbaum Pathologist of the Cook County Hospital for his invaluable assistance in furnishing fresh postmortem material to further the development of the technique

when the "head of the humerus shears off the fibrous capsule of the joint from its attachment to the fibrocartilaginous glenoid ligament"

For the purpose of contrast, we need to review briefly the essential steps employed today in the surgery devised to correct habitual dislocation of the shoulder joint Of the methods that depend upon muscular or tendinous slings for the stabilization of the joint, the Ehrlich-Clairmont myoplasty, and the Nicola tenoplasty are the most widely known The Ehrlich-Clairmont operation utilizes a flap of muscle taken from the posterior aspect of the deltoid muscle and passed anteriorly through the quadrilateral space to be sutured to the tendon of the subscapularis muscle as it inserts on the lesser tuberosity of the humerus Because of its extensive surgery and its frequent failures, this operation fell into disuse The Nicola operation utilizes the long tendon of the biceps muscle to keep the head of the humerus from dislocating from the glenoid fossa After adequate exposure of the shoulder joint, the capsule is opened, and the long tendon is divided below the level of the transverse humeral ligament A tunnel is then drilled from this point of division upward through the head of the humerus to the center of its articular surface The proximal end of the tendon is pulled through the osseous tunnel and reunited with its distal end by interrupted sutures Because of the excessive disruption and trauma to the joint capsule and to the articular surface of the head of the humerus, Berkheiser found it advisable to modify Nicola's operation by drilling vertically and in a downward direction through the lesser tuberosity of the humerus This departure from the original technique eliminates the undesirable step of having to drill through the center of the articular surface of the head of the humerus, but it does not do away with the necessity of laying the joint cavity wide open

Capsulorrhaphy or plication of the capsule has been attempted by many, but seldom found to be curative, and therefore, is never recommended alone Repair of the glenoid ligament alone or in combination with capsule plication and shortening of the subscapularis tendon is also seldom employed



Fig. left. The arm is abducted to 45 degrees and the forearm is in complete supination. The dotted line represents an incision, beginning at the coracoid process and carried down about 3 centimeters from the middle level of the shaft of the humerus.

Fig. 2. Some fibers of the anterior lamina of the tendon of the pectoralis major are cut along its insertion on the lateral aspect of the intertubercular groove.

Of the many procedures that resort to reconstruction of the bony part of the glenoid fossa, those described by Bankart and Oudard are most widely used. In Bankart's operation the coracoid process is divided and drawn downward with its muscle attachments. The subscapularis muscle is severed from its insertion on the lesser tuberosity and drawn inward. After the anterior aspect of the shoulder joint is exposed, the capsule is elevated and kept in position with a small bony wedge. The fibrous capsule is then fixed to the bone along the anterior margin of the glenoid and the subscapularis tendon and the detached coracoid process are reattached.

In the operation designed by Oudard a bony buttress is formed in front of the shoulder joint. He accomplishes this by splitting obliquely the coracoid process and lowering the lateral half on which the tendons of the coracobrachialis and the short head of the biceps are attached, to a point just in front of the glenoid lip of the shoulder joint. Originally Oudard employed a bone graft to increase the length of the coracoid process

when lowering it in front of the shoulder joint.

Of the operations employed today for recurrent dislocations of the shoulder joint, most surgeons believe that the operation devised by Nicola gives the highest percentage of good results. Although this may be true, we must admit that his approach gives less attention to anatomical and physiological considerations than is desirable. The Nicola operation requires the capsule to be laid wide open, the transverse humeral ligament to be cut, and the entire tendon of the long head of the biceps brachii muscle to be displaced from its normal and important anatomical relationship

According to Gray's Anatomy of the Human Body, 1915, vol. 1, "the peculiar relations of the tendon of the long head of the biceps brachii to the shoulder joint appear to require no further purpose. In the first place by its connection with the shoulder and along the smooth humerus the action of the two joints, and also to be elastic ligament to all portions. It strengthens the upper part of the articular surface, and prevents the head of the humerus from being pushed up beyond the acromion, when the deltoid muscle contracts. Thus from the head of the humerus to the center of motion in the glenoid cavity. By its passage along the articular surface it serves to steady the head of the humerus in the various movements of the arm. It lifts the arm, moves from the joint. It connects the supraspinatus and infraspinatus muscles to the head of the humerus in the glenoid cavity, and prevents its slipping over its lower edge, or being displaced by the action of the latissimus dorsi and pectoralis major, as in abduction, and many other such movements."

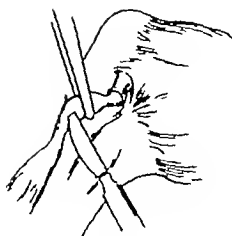


Fig 3

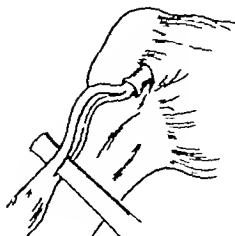


Fig 4

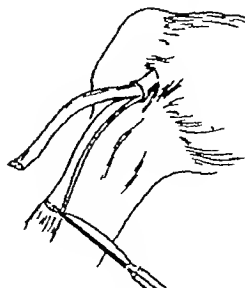


Fig 5

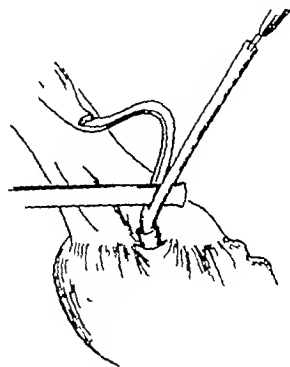


Fig 6

Fig 3 With arm still in abduction, the long tendon of the biceps is split lengthwise into ventral and dorsal halves, by first passing sharp point of scalpel through its central axis

Fig 4 Further splitting of the long tendon with the blunt end of the scalpel

Fig 5 The anterior or ventral half of the split tendon is cut across at its lower end, near the muscle belly

Fig 6 The arm is next adducted, and then it is raised forward and upward to an angle of 135 degrees or more. The intra-articular portion of the long tendon of the biceps is thus exteriorized thereby making it possible to proceed with the visible blunt division of the tendon in a direction toward its attachment on the supraglenoid tubercle.

Another highly undesirable feature of Nicola's procedure is the marked trauma to the articular surface of the humerus when the bit of the drill breaks through that surface, causing jagged edges. Wishing to retain the basic principle of Nicola, yet at the same time being guided more strictly by anatomical considerations in the treatment or stabilization of a shoulder joint subject to recurrent dislocations, the writer set out to devise a method which would reduce to a minimum the interference and trauma to its various components. The technique to be described herein was developed on embalmed and then on fresh autopsy cadavers. Experimentally, the shoulders of fresh cadavers were first dislocated, and then opened. Inspection revealed marked stretching and tearing of the shoulder capsule, especially at its anteroinferior aspect. The author's "extra-articular" operation was carried out, and found to be satisfactory in holding the head of the humerus securely in the glenoid fossa, even when an attempt was made to redislocate it.

THE METHOD

The proposed method of operation is as follows:

With the arm abducted to 45 degrees and the forearm in complete supination (Fig 1), an incision is made from the site of the coracoid process downward to about 5 centimeters from the middle level of the shaft of the humerus, and the deltoid muscle is exposed. The fibers of the deltoid are bluntly split as far down as possible and pulled aside to expose the shoulder joint and the upper one-third of the shaft of the humerus. In order

to uncover completely the long head of the biceps from where it leaves the joint capsule to as far as the muscle belly, some fibers of the anterior lamina of the tendon of the pectoralis major¹ are cut along its insertion on the lateral aspect of the intertubercular groove (Fig 2). Now by flexing the elbow, the long tendon of the biceps relaxes, and it can be easily freed from its loose investing areolar tissue with the blunt end of a scalpel. Once the tendon is lifted from its bed, further gentle stripping frees it along its entire course, from the lower border of the joint capsule to the beginning of the muscle belly. To illustrate the range of sliding of the tendon, the arm is adducted and raised to an angle of about 135 degrees (Fig 6). This maneuver permits the intracapsular portion of the long head of the biceps to emerge for a distance of approximately 5 centimeters or more, thereby making most of it extracapsular. Conversely, by allowing the arm to come down to the side of the trunk again, the originally intra-articular portion of the tendon is seen to glide back into the joint capsule. Proceeding with the operation, the arm is kept in abduction and the elbow is extended, and the forearm is placed in a position halfway between pronation and supination. While the extremity is held in that position,

¹In Cunningham's *Textbook of Anatomy* the description of the insertion of the pectoralis major muscle reads: "The tendon at its insertion forms a fascial expansion which extends upwards over the biceps tendon to the capsule of the shoulder joint. In this way, a bi-laminar tendon is produced, united along its inferior border." While studying the relationship of the insertion to the pectoralis major to the long tendon of the biceps, the writer observed that this tendon, while sliding down through the tunnel provided by the split tendon, is kept closely applied to the surface of the humerus. The latter relationship, therefore, affords an efficient leverage for the long tendon when the biceps brachii contracts.



Fig. 7



Fig. 8



Fig. 9



Fig. 10

Fig. 7. The lower end of the anterior half of the split tendon is fastened with two silk sutures to the eyelet of flexible probe. The other end of the probe is passed through the synovial canal of the tendon almost as far as the supraglenoid tubercle. Here the tip of the probe is pressed upward against the roof of the capsule, and a stab wound is made with scalpel at the point of projection.

Fig. 8. The probe is pulled gently through the opening, bringing through the other end with attached tendon half. A. Represents sagittal section taken through the head and shaft of the humerus in plane that is longitudinal with the canal drilled through the lesser tuberosity.

Fig. 9. The tip of the flexible probe is passed into the newly formed osseous canal until it emerges from the lower opening. The probe is then pulled forcibly through the canal, carrying with it the attached end of the extensor tendon.

Fig. 10. An illustration of the intimate relationship of the displaced tendon to the glenohumeral articulation and capsule of the shoulder joint. A. Further illustrates additional plication of lax capsule by several interrupted Lambert silk sutures. This step invaginates the external half of the long tendon within the external surface of the capsule.

the long tendon of the biceps is split lengthwise into ventral and dorsal halves (Fig. 3, 4). To accomplish this the operator should gently compress the tendon with an anatomical forceps which flattens it lateromedially permitting the scalpel to pass more easily and accurately through its central axis (Fig. 3). The initial passage of the scalpel's point through the tendon is made preferably close to the tendon's exit from the joint capsule. Further splitting of the tendon is continued with the blunt end of the scalpel as far downward as the belly of the biceps muscle and the anterior or ventral half of the split tendon is then severed transversely at its lower end, that is, near the muscle belly (Fig. 5). Additional splitting of the tendon in the upward direction is not attempted until the elbow is flexed, and the arm adducted and then brought forward and upward to more than 135 degrees. This movement exteriorizes the greater portion of the intra-articular portion of the long tendon of the biceps, thereby making it possible to continue the visible blunt division of the tendon, as much as the intact transverse humeral ligament will permit, in the direction proximal, that is, toward the attachment of the tendon on the supraglenoid tubercle (Fig. 6). Then lowering the extremity to the side of the trunk and extending the elbow joint both halves of the split long tendon are seen to slide

back into their intracapsular relationship. Next, the lower end of the anterior half of the split tendon is fastened with a silk suture to the eyelet of a flexible probe and the other end of the probe passed upward through the synovial canal of the tendon almost as far as the supraglenoid tubercle. Here the tip of the probe is pressed upward against the roof of the capsule and a stab wound made with the scalpel at the point of projection (Fig. 7). Then the probe is pulled gently through the opening bringing through the other end with attached tendon half (Fig. 8).

By means of a 5 to 6 millimeter bit, a tunnel is formed in the lesser tuberosity by drilling from its apex vertically downward, that is parallel with the long axis of the humeral shaft for a distance of 3.5 centimeters. The bit is then withdrawn, placed on the outer surface of the tuberosity at an oblique angle with the lower end of that vertical tunnel, and a second tunnel is drilled until it communicates with the vertical one (Fig. 9) so establishing a common canal through the lesser tuberosity. (To break down the crest of bone that might remain at the angle where the two bony tunnels join, as shown at A in Figure 8, the drill bit is moved appropriately to and fro before it is withdrawn.) The tip of the flexible probe is now passed into this newly formed osseous canal until it emerges from the lower opening, and the

probe then pulled forcibly through carrying with it the attached end of the exteriorized tendon (Fig 9)

Before proceeding with the final step, it is important to eliminate completely any wrinkling of the tendon which may have been imparted to it in the course of its handling. Such precaution is secured, when the arm is in adduction and the elbow flexed, by grasping the lower end of the tendon with a hemostat and forcibly pulling it, and at the same time, pushing the head of the humerus toward the glenoid fossa. Having acquired a maximum degree of tautness, the tendon is finally reattached to the intact dorsal half of the biceps tendon by several interrupted silk sutures. Figure 10 illustrates this ultimate relationship of the displaced tendon to the glenohumeral articulation and capsule of the shoulder joint. This figure should indicate also that closer apposition of the head of the humerus to the glenoid fossa is achieved, as well as the re-enforcement of the weakened anterior aspect of the capsule.

The surgical procedure, just described, is one which, in comparison with that of Nicola's, is practically extra-articular (except for the possible tearing of the synovial sheath surrounding the biceps tendon) and, therefore, neither lays open the joint to sepsis nor damages it with subsequent distorting processes. The joint capsule and the transverse humeral ligament are kept intact, and the transplantation of the entire long head of the

biceps muscle from its important relationship is made unnecessary. The time required to carry out the operation is considerably shorter than that for the other operations mentioned. Because of the apparent decrease in trauma one may expect less postoperative fibrosis and consequently a diminution in the number of cases with limitation of motion.

In cases in which a stretched articular capsule exists, the following additional step may be included with definite advantage. Several interrupted Lembert silk sutures are made to invaginate the exteriorized half of the long tendon within the external surface of the capsule, as shown in the insert of a, Figure 10. Such additional plication of the lax capsule not only diminishes the size of the stretched capsule, but also strengthens the displaced tendon in its course down to the upper opening of the osseous canal in the lesser tuberosity.

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removed in quantities of 20 cubic centimeters and was immediately replaced by gas and the post operative care of the patient was carefully standardized in order to provide as constant conditions as possible throughout the study.

Of the 82 patients studied, only 41 were considered reliable enough to report. Some were rejected because they were too young to give dependable answers and others because they were suffering from psychoses which made them unreliable. Patients who gave a history of frequent persistent headaches, vertigo or other symptoms before encephalography were eliminated, as were those whose postencephalographic symptoms disappeared during sleep and hence could not be classified accurately as to the exact time of disappearance.

The results obtained are shown in Figure 1.

From the figures in Table I it is apparent that helium encephalography followed by oxygen inhalation produced symptoms lasting less than half as long as those produced by oxygen encephalography plus oxygen inhalation and about one-fifteenth as long as the symptoms produced by encephalography as it is usually performed with air. It is also apparent from these figures that the effectiveness of postencephalographic oxygen inhalation depends upon concentration of oxygen inhaled, since inhalation of low concentrations had much less effect than inhalation of pure gas.

TABLE I

	Average duration of symptoms—hrs.
Air encephalography followed by	
No oxygen inhalation	53½
Low concentration oxygen	7½
Pure oxygen inhalation	1½
Oxygen encephalography followed by	
No oxygen inhalation	50½
Low concentration oxygen	21
Pure oxygen inhalation	9
Helium encephalography followed by	
No oxygen inhalation	8
Low concentration oxygen	6½
Pure oxygen inhalation	3½

Among the cases reported are 2 in which encephalography was performed by more than one method. One patient suffered for 24 hours after simple air encephalography and for 19 hours after air encephalography followed by inhalation of low concentrations of oxygen. Another patient who suffered for 34 hours after simple air encephalography was symptom-free 3 hours and 45 minutes after helium encephalography followed by inhalation of pure oxygen.

Since this paper was written, all cases in which patients were examined with encephalograms have

been reviewed. It has been noted that in approximately 75 per cent of the cases in which the encephalograms were made under pentothal sodium anesthesia, poor filling of the ventricular system resulted, whereas, in those cases in which encephalograms were performed under local anesthesia, unsatisfactory filling resulted in less than 50 per cent. In 14 cases in which poor filling of the ventricular system resulted under pentothal sodium anesthesia, further encephalographic studies were done under local anesthesia and, in only 1 case were we unable to obtain satisfactory results. As a further check on this, we deliberately used pentothal sodium in 1 case and then, at a later date, repeated the procedure under local anesthesia. In 4 of these cases, no filling of the ventricular system was obtained under pentothal sodium anesthesia, and in 2 others, there was unsatisfactory filling. When repeated under local anesthesia, satisfactory filling was obtained in 9 of the cases and unsatisfactory filling was seen in 1 of the 4 in which there was no air in the ventricles when pentothal sodium was used.

SUMMARY

When the cerebrospinal fluid was replaced by helium gas and the patient was then allowed to inhale pure oxygen until symptom-free, the average duration of symptoms was 3½ hours.

When oxygen was used to replace the cerebrospinal fluid and pure oxygen was then inhaled, the symptoms lasted 9 hours, or more than twice as long.

The symptoms following simple air encephalography as it is usually performed lasted 53½ hours, or almost 3½ days. This is about 3 times as long as the results obtained with helium.

The rationale of helium encephalography is discussed, and various methods of encephalography are compared on the basis of duration of postencephalographic symptoms which they produce.

Pentothal sodium anesthesia has proved unsatisfactory for encephalography. The best results are obtained when local anesthesia only is used preceding spinal puncture. The only advantage of pentothal sodium or general anesthesia is that the patient is not aware of the headache during the immediate procedure.

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CANCER OF THE BREAST

Ten Year End-Results

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THE following is a report of the 10 year end-results of radical operation for cancer of the breast operated upon at the Massachusetts General Hospital during the 5 year period, 1927-1931 inclusive. The cases are the same as those previously reported on a 5 year basis in 1936 and 1939. Several papers on the results of radical operation for cancer of the breast have been published by the author or his associates in the Tumor Clinic on a 5 year basis. A detailed analysis of these cases will not be repeated here (2, 3, 4, 7, 8, 9). In previous reports the patients in the private wards were included with those operated upon in the general hospital. The results have constantly improved since the first study was made in 1907, and the percentage of 5 year cures in the last group studied (1930-1932) was 45 per cent. It was noted that in an appreciable number of cases the recurrence did not appear until after the fifth year, and this review is made to determine, if possible, the number of, and reason for, this late recurrence.

The cases of patients operated upon in the General Hospital only have been studied, for it was deemed too difficult to follow the private patients operated upon by many different surgeons, several of whom are now dead. The results of treatment of cancer have always been found to be better in the patients operated on in private wards, even when the two series are placed in comparable groups as regards duration, extent of disease, histological index of malignancy, age, etc. The reason for this is obscure, but the fact that the prognosis is better in patients who may be said to be in the higher social group has been pointed out by several observers (1, 5, 6, 10, 11, 12). The percentage of 5 year cures is therefore slightly less than that reported in the other communications.

The group studied consisted of 147 cases and with few exceptions these patients were operated upon by members of the tumor clinic staff. The 10 year end-result is known in every case. The usual radical operation was performed consisting of removal of the breast, both pectoral muscles, and the contents of the axilla. A large amount of subcutaneous tissue was removed from the mid-sternal line to the border of the scapula. Sufficient

skin was preserved to allow for primary closure of the wound in most instances, for, as the disease progresses along the deeper lymphatics and not in the skin proper, it is felt that preserving sufficient skin for primary closure is a safe procedure. This has been borne out by the fact that in the 104 cases in which the site of recurrence is known or who are living without disease, there were 6 local recurrences, or 6 per cent.

All patients were carefully studied for evidence of remote metastasis before operation and x-ray films were taken of the lungs and bones to rule out unexpected remote disease. Radical operation was performed only on those patients in whom disease was clinically limited to the breast or breast and axilla. In 5 cases, however, considering the size and extent of the disease, the operation might be considered as palliative.

That estimation of the extent of the disease is subject to considerable error is shown by the fact that 15 patients died within 1 year of remote metastases, the presence of which could not be demonstrated before operation, but without local recurrence. Axillary nodes were involved in all but 1 of these patients and in 3, although the disease was apparently local, it was advanced. Otherwise there was nothing to distinguish this group from certain other cases in which a cure was obtained.

Appraisal of axillary involvement is also subject to considerable error. In this group 84 patients presented axillary nodes clinically, in 72 of which cancer was proved to be present by pathological examination, while in 12 the nodes were inflammatory—an error of 14 per cent. On the other hand in the 63 cases in which no axillary nodes were palpable they were found diseased in 30, representing a 48 per cent error in the clinical appraisal of the extent of the disease. It is felt that the situation of the involved axillary nodes and the number have a distinct bearing on the prognosis, but, unfortunately, these facts could not be determined from the pathological reports.

There were 4 operative deaths—an operative mortality of 2.7 per cent. Three patients died of pulmonary embolus on the 5th, 7th and 21st days respectively, and 1 (colored) of unknown cause on the way to the ward after operation.

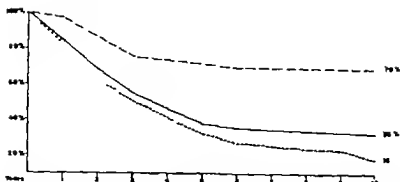


Chart Ten year end results in cancer of breast ——— Total, 34 cases, 33 per cent cures ——— axilla involved, 95 cases, 8 per cent cures ——— axilla not involved, 30 cases, 70 per cent cures (Patients dying of disease 1 end of 10 years considered dead)

The results of operation on a 5 and 1 year basis are shown in Table I. Operative deaths are considered as failures, while patients dying of other causes without evidence of recurrence are excluded as inconclusive.

As will be noted in Table I, 6 patients living at the end of 5 years died later of recurrence, in 9 of whom the nodes were involved. In other words, 9 per cent of the patients living at the end of 5 years will develop late recurrence, or 7 per cent of all patients operated upon considering the patients dying of other causes without disease as inconclusive. In studying the cases further only 1 patient in whom the axillary nodes were negative for cancer died after the 5th year and this patient showed evidence of metastases in the lung and other breast 3 years after operation thus no patient with negative nodes developed recurrence after 5 years. In the 9 patients in whom the axillary nodes showed involvement and who developed late recurrence, all were apparently free of disease at the end of 5 years. In this group there were 30 per cent 5 year cures and 18 per cent 10 year cures. Five lived for 1 year or more after operation and with known recurrence for 4 years.

The 5 year results are approximately the same in the groups previously at died. The number of cases is small and the percentage would be influenced by the manner in which the patients

dying without disease between 5 and 10 years are reckoned.

Further analysis of the cases of late recurrence is not illuminating. The average and median age of the group was 53, the average and median duration of the tumor at the time of operation was 5 months. As to the histological index of malignancy, 7 were classified as of median and 3 of high. The chief sites of recurrence are known in 7 of these 9 cases. The bones were involved 5 times, the supraclavicular nodes 3 times, and the lungs 3 times. There was 1 case only of local recurrence which appeared at the end of the fifth year. Patients living with disease at the end of the tenth year 4 in number are charted as having died in that year (Chart 1).

In 75 per cent of those dying of disease, recurrence and death took place within 3 years of the date of operation.

Sites of recurrence. The site of recurrence is known in 60 of the 88 cases dying of disease, many obviously having multiple metastases. The bones and lungs were the most common sites of metastases, being involved in 29 and 26 instances, respectively. The cervical nodes were the next most common seat, 17 patients having recurrence in that region. Cancer of the other breast, which has been considered as being metastatic, 25 noted in 5 instances. Six per cent only developed local recurrence.

Preoperative irradiation. Twenty-six patients in whom the nodes were involved received pre-

TABLE I — RESULTS OF OPERATION

	Five years 6 (40%)	Ten years 4 (25%)
Living		
Dead		
of disease	7	8
operatively	4	4
Inconclusive		
dead of other cause		
without recurrence	6	3

TABLE II.

	Axilla not involved 5 years 3 (75%)	Axilla not involved 10 years 2 (70%)	Axilla involved 5 years 30 (30%)	Axilla involved 10 years 17 (87%)
Living	3	2	30	17
Dead	4 cases	30 cases	40 cases	95 cases
Inconclusive	3	6	3	7

operative x-ray treatment. Five of these patients are living (19 per cent) while 21 are dead, 20 of whom died within 5 years while 1 lived 11 years. It is only fair to state that the amount of irradiation given to these patients, as judged by today's standards, was totally insufficient seriously to affect tumor cells.

SUMMARY

It would appear from this analysis that in cases of cancer of the breast in which the axillary nodes are not diseased, patients living without clinical evidence of cancer at the end of 5 years may be considered as permanent cures (70 per cent 10 year cures). But, in patients with positive nodes at the time of operation, 19 per cent living at the end of 5 years will eventually die of late recurrence, or 7 per cent of the cases operated upon. These figures might be changed for better or worse if it were not necessary to exclude as inconclusive cases the 13 patients dying of some other

cause before the expiration of 10 years following operation. The results of this study are shown graphically in Chart 1.

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EDITORIALS

SURGERY Gynecology and Obstetrics

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THE PRESENT STATUS OF THE CANCER PROBLEM

SO much has been written on the subject of cancer in recent years that it is not an easy matter to sift out the facts from the near facts and obtain a true picture of progress and actual accomplishment.

As never before the medical profession is increasingly aware that cancer is one of the two greatest and most pressing problems of modern medicine. Heart disease and cancer are our two chief killers. Wilson, of the Harvard School of Public Health, recently found for the first time in the annals of American medicine, that more women during the twenty year span, from thirty five to fifty four years, die of cancer than of any other single disease.

It is obvious that the cancer patient must come to the doctor early in the course of his disease if a cure is to be effected but few realize however that over half of the patients suffering from cancer will not be cured no matter if they go to their physician at the

very first symptom manifestation. Hodgkin disease, leucemia, cancer of the pancreas and of the esophagus, as well as sarcomas of bone offer small chance of cure. And the first symptom of gastric, ovarian, testicular, lung, antrum, and even breast cancer is not infrequently that of metastasis or direct invasion into irremovable vital structures. On the other hand, so much is to be gained from an intensive campaign of cancer control for the other half that does have an opportunity for cure if diagnosis is made early and treatment given that in all probability cancer control which teaches the symptoms and signs of cancer to the laity is our most effective single step in the cure of those who have an opportunity for cure.

The annual physical examination not infrequently reveals cases of both early and late cancer however it has proved to be a disappointment as far as effectiveness goes in finding early cancer.

As a whole, the general public, particularly during the past few years, has learned much about the disease. Widespread fear persists but it is encouraging to note that the last Gallup poll on the subject revealed that 33 per cent of the population now believe that early cancer is curable. The previous Gallup poll had shown that 48 per cent of the population believed early cancer to be curable. There are signs which make us realize that in certain quarters progress is unquestionably being made. It is only recently that McCarthy of the Mayo Clinic, reported that in their cases of operable breast cancer it is necessary to perform a biopsy in three times the number of cases it was fifteen years before. This demonstrates that the mammary cancers of today

are smaller, and therefore more difficult of diagnosis

Although delay from the time of the first symptom until the patient's entry into the hospital for treatment is still appalling, a recent study made at the Memorial Hospital in New York, revealed that twenty years ago, in these same operable breast cases, the average delay was eleven months, seven days, while in 1940 the average delay was four months, seven days—a reduction of 62 per cent in valuable time lost. There are several evidences which demonstrate that the education of the public is catching hold. It is interesting to note two entirely new, and what are proving to be effective, methods of teaching the subject of cancer to the lay public. Five years ago the American Society for the Control of Cancer organized the Women's Field Army Against Cancer. Its chief aim was to enroll women in a campaign, pledging themselves to become informed on the simple signs of cancer, and to take the responsibility for the teaching of this information to the members of their immediate families. This campaign met with signal success. Today there are 225,000 women enrolled in this educational effort, and it is very largely through their influence that much new legislation has been effected, looking to improved care of the indigent cancer patient in several states. It is also the result of their influence that President Roosevelt declared the month of April to be "Cancer Control Month."

The other new experiment is taking place in Westchester County, New York, where a small textbook of seventy-five pages, "Youth Looks at Cancer," is being taught in the biology department of all high schools, and the problem of abnormal growth is being rationally and normally approached.

The program of the Cancer Committee of the American College of Surgeons has been

broad and aggressive. The College gives its stamp of approval to the idea that cancer is such a comprehensive disease that special training in diagnosis, pathology, and treatment is desirable. The College has been effective in establishing 370 cancer clinics in the United States and Canada, representing 20 per cent of the total approved hospitals of 100 beds or over. It is a policy that at the annual Clinical Congress, the subject of cancer shall be presented to the Fellows by a series of papers, by symposia, and by the giving of cancer clinics. Aside from this, the College maintains a registry for cured cancer cases which is available for study. There are now over 36,000 such cases of cured cancer registered. Now that many of the cancer clinics have been established for a period of five years, it is anticipated that the registration of cured cases will proceed at a rapid rate and that the College will soon have 100,000 cases of cured cancer—a monument to the effectiveness of good surgery and sound irradiation.

From the professional point of view, another bright spot is that a comparison of medical school curricula of 1940 with those of 1920 reveals a real increase in the hours allocated to the medical student on the subject of cancer. The medical schools are now beginning to make greater use of their material of the cancer clinics for teaching purposes.

On the whole, sufficient new experience has now accumulated in the fields of surgical and irradiation therapy to make a more exact evaluation of them possible. We now hear less of those extravagant claims which a new and impressive agent inevitably brings out. From experience we now know that there is no place for inadequate or poor surgery in this field. In spite of voluminous literature to the contrary, largely produced by discouraged surgeons and overzealous radiologists, we now find there is no place for incomplete surgery.

being done with the idea that cure of the remaining disease will be effected by irradiation. Radiation is an exact and effective therapy which should be carried out by those familiar with its accomplishments as well as its limitations. In certain pathological states irradiation is more effective than surgery and the reverse also holds true. And there are situations in which a combination of good surgery and expert irradiation offers most.

It seems that at present lead therapy as well as freezing the latest widely heralded cure have been abandoned. The effects on cancerous tissue of the radioactive isotopes, phosphorus and strontium are undergoing critical study. Cancer research laboratories are working ceaselessly on these and other leads. It takes much time and experiment before a cure can be accepted. We must hold fast to those two agents which have proved to be most effective namely "cancer control" and the expert use of surgery, radium, and x rays.

FRANK E. ADAM.

OBSTRUCTIVE JAUNDICE

THE treatment of obstructive jaundice has been shown recently to demand not only especial attention to the preoperative and postoperative care but in addition great care in the selection of the actual operative technique for the case involved. In 1878 J. Martin Sims performed the first premeditated operation on the gall bladder in a jaundiced patient. The patient died apparently from a biliary fistula due to failure to remove the stone from the common duct. The second jaundiced patient was operated upon by W. W. Keen of Philadelphia, and this patient died in 36 hours from hemorrhage, exhaustion, and shock.

The mortality of operations upon jaundiced patients remained high until the twentieth century at which period the emphasis in

surgical study and investigation was placed upon anatomy and pathology. The chief factor in the mortality from operations upon this type of patient was not the result of an insufficient knowledge of pathological anatomy but rather to a lack of knowledge of the fundamental pathological changes in the physiology occurring in the jaundiced state. The work of Rous and McMaster on the bile and extrahepatic bile ducts, and of Rosenfeld, Wells, and Ballman and Mann on the liver were among the first important investigations of this character. With the aid of the information obtained by such studies, certain principles have been formulated regarding the preoperative and postoperative treatment of jaundiced patients with a resulting markedly lowered surgical mortality. That the physiology of this condition is not yet completely understood need hardly be mentioned. Indeed it is but recently that the most important contribution in years has come to the surgeon's aid in the treatment of jaundice—namely vitamin K and bile salts.

Obstructive jaundice to be amenable to surgery must be within reach of the surgeon, either in the common hepatic or the common duct itself. Many of the problems involved in the treatment of such an obstruction are the same irrespective of the type of obstruction. There occurs an increase in the ductal pressure which may be greatly delayed when the gall bladder is normal as in cases of carcinoma of the pancreas. As the pressure approaches 330 millimeters of bile the hepatic secretion of normal bile stops. The bile pigment no longer is secreted into the common duct. The mucous secretion of the bile dilutes the bile already present and the pigment is absorbed. The ducts are thus filled with the "white bile" familiar to us all. It is common knowledge that the presence of "white bile" in the common duct is a bad sign and definite in-

creases the surgical risk. This is true only because it is evidence of liver injury. The pre-operative evaluation of the degree of liver injury is difficult or impossible. A rough idea may be gained by the indirect van den Bergh reaction (degree of jaundice) and the duration of the jaundice. Of the various liver function tests, the hippuric acid test of Quick is probably the best method available at present for determining liver function. In the jaundiced patient, however, the liver damage is evident, but the degree may be questionable. In any event every effort must be directed toward the improvement of the liver function before operation.

For a number of years attention has been centered upon the carbohydrate metabolism in the liver when associated with jaundice. It has been shown that the glycogen stores in this organ are greatly decreased. Therefore, it has become the widespread practice to force the ingestion of carbohydrates in the preparation of these patients for operation. This has, undoubtedly, been very helpful. However, when biopsies were taken of the liver and a number of patients prepared in this manner, it was found that the liver contained a large amount of fat. It has also been shown in experimental animals that the liver glycogen may be increased only by a diligence in the forcing of carbohydrates far beyond that previously taken.

As a result of a series of experiments carried on in the Harrison Research Department of the University of Pennsylvania under the direction of Dr. Ravdin, we have come to believe that the amount of glycogen in the liver is not as important a factor as the amount of fat in the liver at the time of operation. It has been conclusively shown that the degree of liver injury following volatile anesthetics is dependent upon the amount of fat in the liver and not on the

glycogen content. The problem in the pre-operative preparation of the jaundiced patient, therefore, is to remove the fat from the liver as rapidly as possible. Our experimental evidence has demonstrated that this is most effectively done on a diet high both in protein and carbohydrates with no fat. It has been our practice to give a diet in which 14 per cent of the calories are supplied by protein. The rationale of this change from a pure carbohydrate diet to a protein-carbohydrate diet is well founded, for it now seems likely that a great portion of the value received from the carbohydrate regimen used in the past was its ability to spare the protein in the body.

The patients with common duct obstruction frequently have such a reduction in appetite as to constitute a major problem in their pre-operative preparation. Here the feeding of vitamin B and lyophilized bile is helpful at times. In the occasional patient with severe liver injury and a poor appetite, it may even be advisable to pass a tube into the stomach or even into the jejunum and give forced feeding of partly digested protein and carbohydrates.

The most alarming complication in the jaundiced patient is hemorrhage. Before Quick began his studies on the prothrombin in these patients the surgeons were at a total loss to explain why one patient bled and another just as deeply jaundiced did not bleed. Studies of the bleeding and clotting time were of no avail. Now for the first time we apparently have a reliable method of determining the prognosis of the patient regarding the bleeding tendency.

The discovery of vitamin K by Dam and also Amquist has added a new and much needed chapter to the treatment of jaundice. It is now common practice to study the prothrombin of every patient so affected. Vitamin K in some form is fed to the patient

with ample bile salts (sodium desoxycholate) Vitamin K is a lipid and is not absorbed adequately from the intestinal tract in the absence of bile salts. The prothrombin values may be determined day to day so as to follow the improvement, which usually occurs rapidly. It can be anticipated that the prothrombin will fail to rise after such therapy only in patients with jaundice due to severe damage to the liver cell such as probably seldom occurs as the result of common duct obstruction alone. Although vitamin K is a recent addition to the surgeon's armamentarium, its value in the preoperative treatment of these patients is rapidly being established. Certainly the surgeon is no longer justified in operating upon a deeply jaundiced patient without a knowledge of the prothrombin value and the use of vitamin K if it is low.

Before the use of vitamin K the incidence of hemorrhage following operation remained about the same year in and year out. The mortality following these hemorrhages was materially reduced by repeated blood transfusions. Doubtless we shall find patients with severe liver damage who fail to respond to this type of therapy. We believe that such patients will be few. It may be possible to predict and experience may show that a failure to respond to vitamin K therapy will suggest that the jaundice is due to injury to the liver cell rather than to simple common duct obstruction thus eliminating surgery.

The prothrombin may be increased rapidly by blood transfusions. This doubtless accounts for the benefit derived from the multiple small transfusions as used for some years in these cases. Studies by Dr. John Rhoads at the University of Pennsylvania have shown that fresh blood should be used in these transfusions, as "bank blood" loses its prothrombin rapidly. It goes without saying that if the

surgeon is forced into operation upon a patient whose prothrombin does not rise following vitamin K therapy multiple small transfusions of fresh blood, as in the past, continue to be the treatment of choice.

Volatile anesthetics which are toxic to the liver cell should be avoided in the surgery of the jaundiced patient. Nitrous oxide and the barbiturates are also bad because of the anoxemia which frequently accompanies their administration. Ethylene and cyclopropane gases which may be given with a high percentage of oxygen are probably less objectionable although accurate control studies have not been made of these agents in the experimental laboratory. Local anesthesia is undoubtedly the anesthesia of choice from the standpoint of the liver. However it seldom affords sufficient relaxation to carry on the operation required. Its usefulness is definitely limited by the temperament and build of the patient and the temperament and skill of the surgeon. Spinal anesthesia conducted by a physician anesthetist should be considered the anesthesia of choice. It is indubitably an excellent anesthesia, its chief drawback, however being the anoxemia that is associated with the occasional drop in blood pressure. For the same reason surgical shock is to be avoided in these cases.

The postoperative care of the jaundiced patient is a continuation of the preoperative care plus the additional attention to the wound and biliary fistula if established.

It is highly important to continue the patient a nutrition in a usable form. The most acceptable method has been a continuous venoclysis of glucose solution until the patient can retain an adequate intake by mouth. Recent investigations in the experimental animal in the laboratory suggest that the amount of glucose that is usually given by venoclysis is not great enough to give the best

EDITORIALS

results. These experiments have attested to the value of passing a tube into the jejunum before operation so that forced feeding of a high carbohydrate protein may be administered for a few days before and after operation.

The continuation of the antihemorrhage therapy is imperative. Vitamin K should be given and bile salts must be given also since bile salts do not reappear in the bile for a considerable period of time after the release of common duct obstruction. Small transfusions of fresh blood should be given every 8 hours in the most severely jaundiced cases for 2 or 3 days. Vitamins other than K are now being added.

The use of a decompression apparatus in the drainage of the biliary tract may be useful. When only a first stage operation—a cholecystostomy—is done, the pressure in the biliary tract may be reduced gradually in the same manner as in decompression of the urinary tract. This may reduce the possibility of bleeding. When the obstruction has been removed the pressure in the biliary tract will depend upon the duodenal pressure, as for example in the cholecystoduodenostomy. When a T tube has been placed in the common duct the decompression apparatus is helpful

in forcing the bile into the duodenum, rather than allowing it all to escape externally.

If the patient loses a sufficient amount of bile externally there may be a profound biochemical disturbance which is not entirely understood. Unless this bile or its equivalent is given back to the patient he may develop marked listlessness and sudden attacks of a shock-like state with a low blood pressure and cold sweats. Refeeding the bile in its entirety by a slow drip through a tube in the stomach is useful. Lyophilized human bile collected from previous patients and lyophilized pig's bile have recently been used very successfully.

The length of time the T tube should be left in the common duct varies somewhat according to circumstances. In the ordinary case of common duct stone we usually remove it on about the 14th day. The tube is clamped entirely for several days before its removal. In the case of a stricture for which a plastic operation has been done, the tube is left in place for months in an endeavor to minimize further scar contracture.

Space does not permit discussion of surgical procedures incident to the correction of the various types of obstruction which are producing the jaundice.

ELDRIDGE L. ELIAS

THE SURGEON'S LIBRARY

REVIEWS OF NEW BOOKS

MEDICAL men of today surgeons in particular, have long been familiar with the saga of the Mayos—father and sons. To them it has always been an inspiring and stimulating story and they have recognized almost without exception the forceful impetus the Mayo Clinic has given to medical and surgical progress, and what a far-reaching and helpful part it has played in American life for the past 50 years. Even those who know the story best will be grateful for the opportunity to read the complete and well authenticated account of Miss Chapman.

The most forceful appeal of this volume to the reviewer, is in the stimulus it affords and the example it upholds for the medical student of today. Combining Oskar McCollam's *Halstead Watson's Life of Sir Robert Jones The Hero and Busy Doctor* Flexner's *William Henry Welch and how The Doctors* if you are all comparatively recent volumes. They should be in the library of every medical school and hospital. The man with the divine spark burning brightly may not need to know what others before him have achieved, but most of us are not provided with self starters, and a few turns of the crank at the right time can sometimes accomplish wonders.

As to the story itself, it is well told and with not too much flourish and fancy writing. The opening chapters are a little tedious and the account of his toric facts, diligently sought out and verified, are too often elaborated with descriptive passages and generalizations that detract from the directness of the story. With the beginning of the Rochester period the story comes to life and from that moment almost every page except for the elucidation of surgical procedures, is interesting. Gradually one character emerges as the dominating personality that of Will Mayo and though the picture of Dr. Charlie, the lovable and understanding surgeon, the skillful technician, the much sought after "trouble shooter" is skillfully portrayed, it is Dr. Will who finally holds the center of the stage.

"Stress the tim and the opportunity said Dr. Will to his biographer. We were reared in medicine. There were three of us. All well and good but at the center of every effective effort in this world of ours, whether for good or evil, there is one individual who provides the divine fire that kindles and burns and, sometimes, tests a co-flagration. Such an individual was Dr. Will Mayo and in reading *The Doctors* if you one cannot help but conclude that the outcome would have been the same whether his lot had fallen in Rochester in

Boston, or in London. His debt to others freely acknowledged, was great, but so is that of any other leader of men.

The most arresting incident of the volume is that briefly told on page 608, "I've just done my last operation." To take off the mantle, worn so long, valiantly and gracefully to pass it on to younger men, and to bid them Godspeed and to do it without a sign of self-pity—in that act are all the elements of drama—heroism, renunciation, forgetfulness of self. Of men with the ideals and force of characters of Dr. Will and Dr. Charlie the medical profession has every right to be proud.

The review in more detail, book so interesting and stimulating is needless. Every medical student and every doctor will find in it interest, humor and inspiration. And the young man in particular can recall Napoleon's words. Every French soldier carries in his knapsack the baton of Charlemagne of France.

SEYMOUR L. KOC.

TOBIAS has turned out an excellent volume giving the essentials of dermatology. The material is up-to-date, is authentic for the day, and is presented in a clear, succinct manner. The book presents to no more than brief treatise so that it does not contain references to pertinent literature, etymological notes, or statistical facts. The volume is sparsely illustrated, but the illustrations that are shown are well chosen and are all in black and white. The basic principles of diagnosis and treatment are adequately considered and there is included even definitions of the more rare dermatoses. The book should prove to be very useful to the student and the practitioner as all of the common cutaneous diseases are treated quite adequately although the text is brief. The one criticism that I would make is the paucity of photographs. Those that are included are excellent but I believe the book would have a great deal more merit with a few more photographs of the commoner skin diseases. This criticism is negligible in relation to the book as a whole. It deserves fair reception for it is one of the best of the smaller introductions.

EDWARD A. CURTIS

THE lectures of Lawson Brown on the history of tuberculosis are an important part of the courses in the Trudeau School of Tuberculosis. They have been perpetuated in a volume entitled *The Story of Chronic Pulmonary Tuberculosis*, which contains the lectures posthumously edited by Miss Chapman.

CHRONIC PULMONARY TUBERCULOSIS. By Lawson Brown, M.D. Philadelphia: The University of Pennsylvania Press, 1941.

The Doctors Mayo. By Helen Chapman. Minneapolis: The University of Minnesota Press, 1941.

Brown With the exception of the chapter on x-ray by Homer L. Sampson and that on chest surgery by Edward W. Archibald, the material is essentially in the inimitable manner of Dr. Brown. The 381 pages present an intensely interesting parade of the historical background of the refinements in chest examination and the study of tuberculosis.

The delightful narrative style makes the book a pleasure to read. It is a source book of early history in which the author has gleaned the facts from a lifetime of reading. The bibliography is quite complete and representative. The volume is well indexed both by subject and author titles. This is a good practical volume and should be in the library of anyone interested in clinical tuberculosis or the history of medicine.

E. L. WALSH

IT is with great satisfaction that the reviewer studies a new text on endocrinology. Grollman's *Essentials of Endocrinology*¹ is a moderate sized single volume compilation written for the medical student or anyone wishing to get a general scientific grasp of the endocrine field. Other works on this subject have suffered from specialization upon one gland or, on the contrary, because the author has presented a diffuse clinical picture with excessive therapeutic claims. The present volume is a complete scientific epitome of present endocrine knowledge. There are some passages and some conditions in the work that can be criticized, there are occasions when contradictions seem to be presented, for instance, in the discussion of "dwarfism due to pituitary insufficiency" it is emphasized that the appearance is one of "precocious senility," but in the illustration of a typical case of pituitary dwarfism the "juvenile appearance" is pointed out. On the whole, the discussion is brief and precise, description of syndromes is necessarily abbreviated, physiology and pathology are accurately stated and therapy is presented in a conservative manner but with encouragement when warranted.

PAUL STARR

THE monograph on *Orbital Tumors*² by Dandy consists principally of a review of the histories of 25 patients with operable and 7 with nonoperable tumors of the orbit, all verified microscopically. These tumors included fibromas, osteomas, meningiomas, sarcomas, carcinomas, gliomas, osteomatous cysts, Schueller Christians's disease, and inflammatory masses. Hyperostosing meningiomas were present in greatest number (9), and Schueller Christians's disease was second in numerical prominence (5). An account of the patient's complaints and neurological signs, the operative note, and a brief histological discussion accompany the presentation of each case history.

The operative approach was in most instances a modification of that used by most neurological surgeons in their attack upon orbital tumors. Dandy

uses a "concealed skin incision" to effect a trans-frontal osteoplastic flap, placed somewhat laterally in the frontal region. The advantages of the transcranial approach over the Kroenlein and other external orbital approaches is pointed out, and the accessibility of the orbital contents and the possibility for complete removal of the tumor without incidental damage to orbital nerves, vessels, and muscles is attested to by the improvement in the patients and the nonrecurrence of the tumors after the patients had been followed for many years by the author.

The outstanding feature of the book is unquestionably its fine illustrations. They alone could tell the story. The artist's sketches of the tumors *in situ* as well as the operative sketches are excellent. The photographs of the patients before and after operation, of the tumor specimens both gross and microscopic, and of the x-ray pictures of the skull indicate how long, carefully, and patiently the author collected his illustrative material. Several of the case histories are made spectacular by the illustrations alone.

JOHN MARTIN

A SYMPOSIUM delivered at Vanderbilt University in April, 1941 has been published as *Infantile Paralysis*³ by the National Foundation for Infantile Paralysis, Inc. The purpose of the meeting as set forth in the preface was to inform the medical profession and the public the "extent of advance and the limitations of the contributions of science to the solution of the manifold and intricate problems of poliomyelitis."

The book is written in sections by six contributors. "History of Poliomyelitis up to the Present Time" by Paul F. Clark, Ph.D., "The Etiology of Poliomyelitis" by Charles Armstrong, M.D., "Immunological and Serological Phenomena in Poliomyelitis" by Thomas M. Rivers, M.D., "The Pathology and Pathogenesis of Poliomyelitis" by Ernest W. Goodpasture, M.D., "The Epidemiology of Poliomyelitis" by John R. Paul, M.D., "The Treatment and Rehabilitation of the Poliomyelitis Patient" by Frank R. Ober, M.D.

The literature is comprehensively reviewed, but the authors do not clarify the issues so that one unversed in virus diseases can obtain a clear picture. The result is the impression that nearly all claims for progress in the study of poliomyelitis have been refuted. Such, of course, is not the fact. Here and there is an island of crystallized thought, but too often the few truths about poliomyelitis are lost in the discussion. The consensus of the authors is that the research has reached a plateau, that, despite much effort, nothing new has been discovered for some time, and that we must develop new methods of investigation.

As a review intended for the general practitioner, the book does not fulfill its purpose. There is too

¹ESSENTIALS OF ENDOCRINOLOGY. By Arthur Grollman. Ph.D., M.D. Philadelphia: London: Montreal: J. B. Lippincott Co. 1941.
²ORBITAL TUMORS, RESULTS FOLLOWING THE TRANSCRANIAL OPERATIVE ATTACK. By Walter E. Dandy. New York: Oskar Pfister. 1941.

³INFANTILE PARALYSIS. A SYMPOSIUM DELIVERED AT VANDERBILT UNIVERSITY IN APRIL, 1941. New York: The National Foundation for Infantile Paralysis, Inc. 1941.

much detail of experimental work. The sections are repetitions and overlap considerably. No contributor seems completely aware of the productions of his fellow hence the duplications. The literature is so completely covered that the reader is confused by the number of quotations and the paucity of conclusions that may be derived.

The book leaves the reader flat. Certainly after one notes the names of the contributors he is disappointed in the content of their lectures. The lack of integration between sections furthers the feeling that clearer picture could have been presented.

A redeeming feature is the rich bibliography valuable for one interested in the details of the experiences of the investigators of infantile paralysis. However as a book intended to present the current status of the knowledge of this disease to the physician, health officer and ultimately the public, the symposium falls short of the mark.

BENJAMIN BOWEN.

THE book *Abdominal Surgery of Infancy and Childhood* by Dr. William E. Ladd and Dr. Robert E. Gross of Boston, recently published by W. B. Saunders of Philadelphia, is without question the outstanding work in this field with due respect to that of Barrington Ward of England, published in 1937.

Some books on surgery are of value not because they express the opinions of the author but because they cover an exhaustive review of the literature and, therefore, include a variety of leading opinions. Such books, unfortunately often confuse the reader and leave him quite in doubt as to the best methods of procedure. Other books are of value because they convey almost exclusively the opinions of the author himself, opinions based on a wide experience in his field over a long period of time, references to the literature being incidental. This book by Dr. Ladd and his younger associate Dr. Gross is an outstanding example of the latter type of work, inasmuch as it is the product of the life work of the men whom we all recognize as the leader in this country if not in the world, in the realm of children's surgery.

Expressed in simple, clear cut language which is easy to read, accompanied by admirable photographs, excellent drawings, and clear ray films, the authors convey to the reader the data on their own experiences or others of their staff during the past 3 years at the Children's Hospital in Boston, each chapter covering the etiology pathology clinical symptoms diagnosis and the types of treatment they have found most useful. Invariably the authors have concluded each of the 36 chapters by a brief summary of the end-results which have been obtained by a long period of follow-up.

I have the impression after carefully reading this book that it is of inestimable value not only to the young students of medicine and the men in general

practice but to all those who have a special interest in this field, whether he be a pediatrician or surgeon.
EDWIN M. MILLER

THE admirable monograph *Lymphatics, Lymph and Lymphoid Tissue* by Drinker and Voegey represents an elaborate extension of the original monograph of Drinker and Field on *The Lymphatics, Lymph and Tissue Fluid* (1933). The new monograph contains a section dealing with lymphoid tissue and a chapter on the electrolytes of lymph, written by D. A. B. Hastings. This monograph is uniquely complete in its clear and succinct presentation of what is known of the significant anatomical and physiological aspects of the subject and its discussion of the clinical problems which daily arise in the mind of the physician. A large amount of data is presented and all the subject matter is critically analyzed. Facts are separated from fancy and the error of uncertainty of a number of current notions regarding the lymphatic system is exposed. The monograph should be read by every student of physiology bacteriology and pathology. It is highly recommended to the surgeon and the internist; however, the general practitioner and the specialist, regardless of his degree of specialization, will also find information that will assist him in his everyday practice.
A. C. IV

IN the third edition of *Body Mechanics in Health and Disease* the authors give greater attention to the prevention of deformities which have their body mechanics as their underlying cause. A new chapter on developmental deformities is added and some of the chapters, wholly rewritten, include the conception that the maintenance of physical fitness and health is important in the prevention of developmental deformities. A practical application of this conception is illustrated with case reports. The instructions for exercises have been entirely rewritten. The clarity, diction, and style with which poor body mechanics is described are commendable.

Body types and body mechanics are described. Back strains as well as alterations of the circulatory system are discussed. There are chapters concerning cardiac conditions written by Kerr with description of the Kerr Lager belt, chapters concerning the diseases of the abdominal viscera and one about the diseases of the nervous system, a chapter discussing chronic arthritis with especial regard to postural disturbance.

Cases of diseases of the nervous system including multiple sclerosis and muscular dystrophies are cited. They show the treatment for improved posture and the symptoms relieved. The value of improved

NERVOUS, LYMPH, AND LYMPHOID TISSUE. THEIR PHYSIOLOGY AND CLINICAL SIGNIFICANCE. By Dr. E. Drinker, M.D., Sc.D., and Joseph Marshall Voegey, M.Sc., M.D. F.A.C.S. (Lond.) Cambridge Massachusetts: Harvard University Press, 1941.
THEY INCLUDE A CHAPTER ON LYMPHOID TISSUE. By Joel E. Goldhamer, M.D., F.A.C.S. L.D. Lloyd J. Hastings, M.D., F.A.C.S. Lister Institute, London, and John G. Wilson, M.D., F.A.C.S. With chapters on the Heart and Circulation as Related to Body Mechanics. By E. C. IV, M.D., F.C.T. 36 of Philadelphia, London, and Montreal J. Lippincott Co. 1941.

ABDOMINAL SURGERY OF INFANCY AND CHILDHOOD. By William E. Ladd, M.D. F.A.C.S. and Robert E. Gross, M.D. Philadelphia and London: W. B. Saunders Co. 1941.

body mechanics in the treatment of chronic arthritis as well as in prophylaxis, particularly in the hypertrophic type, is emphasized. The treatment requires understanding of these chronic conditions, it requires patience and time, but it offers help to individuals who are otherwise neglected and permitted to suffer, with the consequent advancement of the illness and increased loss of function.

Nothing is said of the cause of poor posture. Poor posture is apparently assumed to be primary. The results obtained by the authors are in accord with the conception that poor posture is secondary to the functional decompensation, that the altered posture itself then is a factor in decreasing functional capacity. Correction of the deformity will improve functional capacity, and removal of strain as well as increase of strength will re-establish normal function with relief of symptoms. The value of vitamins and minerals is granted in certain cases, as well as the diet to diminish excess weight and thus decrease the load. The importance of good foot statics for body mechanics is stressed, but the authors advise the use of supports as a means of treatment instead of correction of the altered position and re-establishment by means of normal functional exercise, namely, correct gait.

The application of the concepts brought forth is practical as is demonstrated by the case reports which show what can be accomplished by the use of treatment for impaired body posture in chronic cases. The importance of good body mechanics in the maintenance of physical fitness and health is emphasized.

This is a basic book for the orthopedic surgeon and is recommended to physical therapists, physical education teachers, public health physicians and nurses, and to internists, especially those interested in chronic diseases.

EMIL D W HAUSER

THE development and experiences in England of the Health of Munition Workers Committee from its inception in 1915 through to the establishment of the Industrial Health Research Board is traced in Vernon's *The Health and Efficiency of Munition Workers*.¹ It depicts a prolonged, intensive study of the complexities of the human element in industry. As such, experiences in hours of work, rest periods, night shifts, sickness and absenteeism, accidents, fatigue, ventilation, heating, lighting, welfare problems, and their relationship to employee efficiency are related. These problems are considered in the light of data accumulated in World War I, peacetime in private industry, and the experiences of today.

The book is of great interest to those of industrial management interested in industrial relations, employee welfare and safety education. As a reference work in a library of industrial medicine it is of value,

¹THE HEALTH AND EFFICIENCY OF MUNITION WORKERS. By H M Vernon M.A. M.D. London: Humphrey Milford (Oxford University Press) 1940.

to one, however, just casually interested in industrial practice, it is only of limited interest.

E L WALSH

THE contents of Bancroft's *Operative Surgery*² deal with the surgical treatment of abdominal diseases and, with the exception of the section on spleen, do not deal with etiology, pathology, or diagnosis. Comprising 20 sections by as many widely known contributors, the work represents a distinctive departure from previous similar works, because of the uniformly splendid character of each section and because a complete treatise on the operative surgery of the abdomen is contained within one volume.

Section I concerns anesthesia, preanesthesia, drugs, inhalation, rectal, spinal and regional anesthesia. Section II concerns preoperative and postoperative treatment and is an extraordinarily fine and complete exposition of fluid balance, chemistry, shock, vitamin therapy in abdominal surgery, and hypoproteinemia. Section III covers blood transfusion. Section IV about the general principles of surgical technique, skin preparation, sutures, hemostasis, etc., attracted the attention of the reviewer because it is fascinating reading. There follow sections on the mouth, including neck dissections, a section on abdominal incisions, in which there is an interesting exposition of and argument for the transverse as opposed to the longitudinal incision. The remaining sections are exclusively about abdominal conditions and in the following order include peritonitis, gastroscopy, stomach and duodenum, jejunal ulcer, small bowel, appendicitis, colon and rectum, anus, bile tracts, liver, pancreas, spleen, and diet in postoperative abdominal conditions.

Avoiding vague generalities of praise, certain specific comments should be made. Practically all operative procedures suggested throughout all sections conform to the generally accepted ideas thereon. The chapters relative to peritonitis, stomach, duodenum, appendicitis, small bowel obstruction, colon, bile tracts, and spleen are worthy of special mention in this respect. The once common practice in such volumes of including much obsolete material for completeness, often to the confusion of the younger surgeon, is lacking. The illustrations, for the most part line drawings, are excellent. The subject matter is presented in a most interesting fashion. The book represents a valuable contribution as a compact reference work on abdominal surgery.

J R BUCHBINDER

IN a well written monograph³ of 257 pages Spink presents in a clear, concise manner the use of the sulfonamides in the practice of medicine and surgery.

²OPERATIVE SURGERY INCLUDING ANESTHESIA PRE AND POST-OPERATIVE TREATMENT PRINCIPLES OF SURGICAL TECHNIQUE BLOOD TRANSFUSION AND ABDOMINAL SURGERY. Edited by Frederick W Bancroft A.B. M.D. F.A.C.S. New York and London: D Appleton Century Co. Inc. 1941.

³SULFANYLAMIDE AND RELATED COMPOUNDS IN GENERAL PRACTICE. By Wesley W Spink M.D. Chicago: The Year Book Publishers Inc. 1941.

an excellent chance of being labeled endothelioma, and in no case has the origin of a tumor from endothelium been proved.

Furthermore much confusion has arisen because of the uncertainty concerning what should be called endothelium. According to Maximow and Bloom, the term should be reserved for the single layer of squamous cells which line the inner surface of the walls of the blood and lymph vessels and of the heart. MacCallum believed that only the lining cells of the blood and lymph vessels can be accepted as endothelium and stated that a few true endothelial tumors have been described which appear to arise from endothelium of blood vessels. Borst, on the other hand interpreted the term very broadly and accepted the endothelial origin of a wide variety of tumors whose exact nature has not been determined. Ewing (16) while admitting deficiencies of our present knowledge stated that his own experience inclined him to pursue a similar course.

It is evident, however from an analysis of the recent literature that many pathologists today agree that the term endothelioma has had too wide an application. In their opinion the term should be restricted to tumors arising from blood and lymphatic vessels and having vasoformative characteristics. The basis for this interpretation can best be understood in the light of the modern embryological conception of the origin and development of endothelium and of the vascular system.

EMBRYOLOGY

Endothelium arises from embryonic connective tissue, the mesenchyme which is a derivative of mesoderm. Other derivatives of mesoderm similar to endothelium are *mesothelium* which forms the lining of serous surfaces (pleura, etc.) and *mesenchymal epithelium* which gives rise to the lining of the meninges (49). These tissues, while similar in structure have very different developmental potentialities. In the early embryonic development endothelium arises through the flattening of undifferentiated mesenchymal cells but in the adult it is a highly differentiated tissue which grows only through proliferation of its own elements. Blood vessels and blood cells arise from the primitive endothelial cells shortly

after the formation of the germ layer probably coincidentally and successively at many foci in the embryo (theory of local origin). Blood vessels form by liquefaction, vacuolation, and flattening of the primitive endothelial cells. The vessels grow by proliferation of the endothelial cells and a process of budding or sprouting takes place. The vascular endothelium loses its blood forming power early and is transformed into the highly differentiated vascular endothelium of the adult organism. Lymph vessels also are of endothelial origin probably arising from mesenchyme independently of blood vessels (51).

Maximow and Bloom make the significant statement that in the adult form it is often impossible to differentiate squamous cells of mesenchymal origin (endothelium) and those of ectodermal or entodermal origin. Adult cells similar in structure and arrangement may have a totally different embryonic origin and quite different developmental potentialities. For this reason attempts to identify and classify neoplasms of the so called endothelial group have proved difficult and controversial. Only by careful consideration of these embryological factors and by a thorough study of the histogenesis as well as the morphology is it possible to diagnose accurately these tumors of endothelial origin.

HISTOGENESIS

Since vascular tumors vary greatly in their growth and development, interpretation of their histogenesis is difficult and confusing. Many excellent reports on the histogenesis of vascular tumors are found in journals devoted to dermatology and pathology. The authors, while not entirely in accord in their interpretations and conclusions, give detailed discussions of the histological and developmental variations in these complex tumors, emphasizing the importance of origin and development in their classification.

An analysis of these studies indicates that, on the one hand, there occurs a typical benign angioma of the cavernous or capillary type which is a highly differentiated structure composed of fully developed adult blood vessels. This tumor grows slowly with little evidence of cellular activity. On the other hand, there

is a rapidly growing, invasive, metastasizing tumor consisting of angioblastic tissue which is embryonic in type and very cellular. It has little structural differentiation and is definitely malignant. Between these two extremes there are tumors with varying degrees of cellular activity and differentiation, some of which may become malignant clinically, although they appear relatively benign histologically.

Simple benign angioma is a tumor composed essentially of blood vessels which grow independently and have no intimate anastomotic connection with the circulation of the part. It must be differentiated from hypertrophic granulation tissue which follows inflammation and from mere vascular dilatation seen in chronic varicosities. Benign angiomas are congenital tumors, tracing their origin to the first anlage of the vascular system in early embryonic life (63). Some writers include them in the class of congenital malformations due to developmental errors or fetal displacements without power of proliferation, such as the "hamartoma" of Albrecht. Jaffe stated, "This tumor is a hamartoma with a tendency to continuous growth." Reid in a report on arteriovenous communications expressed the opinion that many angiomas represent congenital abnormal communications between the smaller arteries and veins. However, most agree with Ribbert that angioma, though congenital in origin, is a true neoplasm which grows independently from its own vascular substance and may invade surrounding structures.

The origin and growth of benign angiomas have been studied and analyzed by many authors. Their growth resembles very closely the development of vascular tissue from primitive vasoformative cells (vascular endothelium) in the embryo. The lining cells of the tumor capillaries proliferate and extend as buds or processes, probably from multiple foci, into neighboring tissue. The tumor cells become vacuolated. The vacuoles of adjacent cells coalesce to form irregular spaces which later contain blood. In many tumors these spaces remain more or less irregular in shape (cavernous angioma), in others the lining cells become arranged as a definite endothelium and practically normal capillaries are formed (capillary angioma).

It is well known that benign angiomas often undergo spontaneous regression or healing. Thrombosis of the blood spaces occurs, followed by organization and even calcification, as indicated by the presence of phleboliths. Capillary angiomas that grow very slowly may contain vessels of adult character in which the endothelial spaces are surrounded by smooth muscle and fibrous tissue, an organoid variety of angioma (24). Such tumors offer little difficulty for recognition and classification. When the cellular activity, however, becomes such that the open spaces give way to solid masses of compact endothelium-like tissue, interpretation and classification become difficult and controversial. Invasion of adjacent tissue, local recurrence, and metastasis further complicate the picture.

A group of angiomas has been described which appears benign histologically but which behaves clinically in a manner suggestive of a malignant growth as indicated by local invasion and destruction, recurrence after surgical removal, and metastasis to distant organs. This tumor has been variously designated as benign metastasizing angioma (6), multiple mesenchymal hemendothelioma (61), malignant mesenchymal angioma (39). It presents a manifold histological appearance with transitional stages, varying between undifferentiated mesenchymal tissue and mature adult blood vessels.

There is considerable controversy in the literature concerning whether or not these apparently malignant growths can actually develop from the more benign forms, and whether the presence of multiple tumors actually represents metastases. Many authorities report cases in which metastasis occurred. Jaffe, on the other hand, doubts the existence of benign metastasizing angioma and believes that these cases of multiple tumors do not represent true metastases. It is his opinion that they arise coincidentally and independently of each other from multiple congenital foci.

There is much evidence to indicate that in the malignant angiomas there is a tendency for the undifferentiated mesenchyme to form other structures of mesenchymal origin, differing from true endothelium. It may form connective tissue with a structure suggesting

sarcoma, or an epithelium-like structure with alveolar formation suggesting carcinoma. Such a process offers a logical explanation for the development of the "angioendothelioma" of bone, described by Kolodny which is an epithelium-like tumor closely resembling metastatic carcinoma or hypernephroma, and which will be discussed in more detail.

To summarize vascular tumors are mesenchymal in origin probably growing from congenital rests by a process of endothelial proliferation and differentiation into blood vessels. They are usually benign and may undergo regression and healing. True malignant angiomas exist, however characterized by rapid growth, invasion of surrounding tissues, and metastasis. Such tumors in their histogenesis tend to revert to the original primitive mesenchymal tissue producing a varied histological picture differing greatly from that of the benign, well differentiated form. They may possess morphological characteristics of either epithelial tissue (carcinoma) or mesodermal tissue (sarcoma). There is one essential feature, however which persists throughout the process no matter how varied or bizarre it may be, the recognition of which is essential for the diagnosis and differentiation of tumors of vascular origin. *An angioblastic tendency as evidenced by a vasoformative process of endothelial proliferation and the formation of new blood vessels must be present.*

CLASSIFICATION

It is evident from the foregoing description that the complex and varied histogenic and morphological picture presented by these tumors makes their classification and terminology difficult, confusing, and controversial. It is well known that the classification and nomenclature of any neoplasm has been a difficult problem, and in no other group has this been more evident than with endotheliomas. As a result, many methods and systems of classification have been advocated some of them are inadequate and others too complex and confusing. Restricting the term endothelioma to tumors of vascular origin with a definite recognizable vasoformative tendency simplifies the problem to a considerable degree however

Most pathologists classify tumors according to the predominant cell, considering both its structure and its embryonic origin. Mallory stated that the type cell is the one important element in every tumor. Ewing (16) discussed the problem as follows: "The generally accepted plan of classification and terminology which is based on histology modified as much as possible by histogenesis, is a natural product which has become very firmly established and probably deserves to prevail against the varying prominence of embryology, chemistry and etiology."

MacCarty proposed a terminology based on a biological conception of neoplasm, which emphasizes structure, cellular differentiation, and the significance of the reserve cells. Pulford applied this conception to the differentiation of endothelioma, and suggested that the embryonic connective tissue cell (mesenchyme) is the reserve cell of the endothelium. He divided endothelial tumors into three distinct groups: angiomas, angioendotheliomas, and endotheliomas. He considered angioendotheliomas as a connecting link between the benign angiomas and the malignant endotheliomas, and reported a case in which the change from the benign to the malignant in different stages was shown. All three groups were characterized by differentiation into blood vessels.

Fraser classified vascular tumors into compact, capillary, and cavernous types, the compact representing the more cellular or malignant stage. Kettle and Roes suggested a somewhat similar division but pointed out that certain atypical forms occur in which the endothelial cell loses its characteristic features and reverts to an embryonic form, growing as a spindle cell (connective tissue) or it may develop into a flattened pavement cell with alveolar arrangement (epithelium). Busman noted a similar tendency and considered the term endothelioma to represent a compromise between what is histogenically a sarcoma but morphologically a carcinoma. Klinge divided vascular tumors into congenital hamartomas, and genuine vascular tumors which are true neoplasms derived from the mesenchyme. He further subdivided the second group into tumors still showing the mesenchymal tissue

characteristics, which he called malignant mesenchymal angioma, and tumors which arise from the products of the differentiation of the mesenchyme, namely, the true angiomas, and the angioendotheliomas. This problem of terminology and classification of vascular tumors has also been discussed by Geschickter and Keasbey, 24, Rintelen, Rabsom, and Watson and McCarthy.

There is considerable confusion and vagueness in the use of the terms angioendothelioma and angiosarcoma which have been loosely applied to various types of malignant tumors of extreme vascularity. The problem is complicated by the fact that in certain neoplasms there is an excessive development of blood vessels as a result of venous stasis or nutritional demands. These are not true vascular tumors, although their vascularity has been indicated by the term "angiomatous" (16). Many of the earlier reports of malignant angiomas are tumors of this type. Ribbert stated that malignant angioma (angiosarcoma) and angioendothelioma are difficult to differentiate, and that malignant angiomas may very well be called angioendothelioma because in both there is proliferating endothelium which produces vascular channels and invades surrounding structures. Winkler considered angiosarcoma, endothelioma, perithelioma, and angioendothelioma, and sarcoma of vascular tissue as synonymous terms. Borst suggested the term angioblastic sarcoma or malignant angioblastoma as indicating a malignant tumor in which the characteristics of the normal vascular tissue are more or less apparent, although distorted and atypical. Ewing (16) stated that the present tendency is to limit the term angiosarcoma to cellular angiomas in which the unit is the vessel and not the endothelial cell. He reserved the term angioendothelioma for vascular tumors in which the endothelial cell predominates. In discussing the malignancy of vascular tumors, Geschickter and Keasbey (24) stated, "The pathologic conception of malignant tumors of blood vessels (endotheliomas) has been constantly narrowed. Many of the lesions formerly described as hemangioendotheliomas, peritheliomas, cylindroma, and perithelial angiosarcoma may be reclassified as metastatic lesions

of the thyroid or kidney, or as secondary deposits from nonpigmented malignant melanomas."

It is suggested from this study that a simple and workable classification is one which considers vascular tumors as endotheliomas accompanied by a definite vasoformative tendency with endothelial proliferation and new blood vessel formation. These tumors may be classified as (1) benign angioma, a slow growing, highly differentiated tumor, congenital in origin, with definite well formed blood vessels and an innate tendency to regress and heal, and (2) malignant angioma, a more cellular and compact growth with active endothelial proliferation and invasiveness, showing a tendency to revert to its primitive mesenchymal structure. In certain cases of malignant angioma it is possible to differentiate two subdivisions, namely the *angioendothelioma* and the *angiosarcoma*. The angioendothelioma shows a rather marked cellular proliferation, and in its tendency to revert to a primitive mesenchymal structure the cells assume a cuboidal appearance and alveolar arrangement closely resembling epithelial tissue. Nevertheless, new blood vessel formation is evident. In angiosarcoma the vasoformative tendency is much more prominent. This new vessel formation is the predominant feature of the tumor, and enables it to be more easily identified as a true vascular tumor.

These terms are rather indefinite and ill defined, tending to merge one into the other. Structures suggesting both types may be found in different areas of the same tumor, and the terms are frequently used synonymously. Certain clinical features as well as the histogenesis and morphology must be considered in the final analysis. The special clinical and pathological features which apply in the identification and classification of vascular tumors occurring in bone will be considered later.

VASCULAR TUMORS OF BONE

Primary vascular tumors of bone are not common but probably occur more frequently than reported cases indicate. In the benign forms they are slow growing or regressive, and because they are symptomless, they may be unrecognized. In the more malignant types

they present such a varied clinical course and pathologic appearance that they are often incorrectly diagnosed. On the other hand many tumors of bone have previously been included in this group which in the light of further analysis do not belong there.

REVIEW OF LITERATURE

Very few thorough, comprehensive studies of the pathological and clinical features of vascular tumors occurring in bone have been reported in the literature. Most contributions have been case reports or have dealt only with certain special features of these tumors such as the roentgenographic considerations. Many of the older studies are of little value as the majority of the cases reported were highly vascular tumors of various types other than true angiomata.

Hitzrot in 1917 reported a case of cavernous hemangioma of the upper end of the humerus and included the first roentgenograms published on this tumor. He reviewed the literature to 1917. In 1930 Bucy and Capp (10) gave an excellent report on primary angioma of bone with special reference to roentgenographic diagnosis. They reviewed all reported cases to date and added 8 cases, 6 of which were from the Registry of Bone Sarcoma of the American College of Surgeons. Geschickter and Maseritis (17) in 1938 again brought the literature up to date and included 4 additional cases.

Cases of angioma of vertebrae with clinical symptoms have been reported with increasing frequency in recent years. Many have been diagnosed before operation by the characteristic roentgenographic appearance. Topfer in 1928 found angioma of the vertebrae in 257 cases of 2,154 postmortem examinations of the vertebral column: 11.9 per cent. None of the lesions found at autopsy had apparently produced clinical symptoms.

Many cases of angioendothelioma are described in the literature, some of which are included under the term endothelioma. Endothelioma of bone was probably first described by Lucke in 1866. Marchwald in 1895 reported a rather remarkable case of multiple intravascular endothelioma in most of the bones of the skeleton. Howard and Crile in

1905 analyzed 19 previously reported cases and added 4 of their own. Many more cases of single and multiple endotheliomas of bone have been reported but no effort has been made to enumerate all of them here. Hirsch and Ryerson in 1926 gave a complete list of all reported cases. After a critical analysis of these cases they concluded that in many of them doubt exists regarding the thoroughness and completeness of the postmortem examination. In their opinion many of the tumors reported as endotheliomas were no doubt metastatic carcinoma from primary lesions not found at autopsy.

Kolodny in 1926 reported 2 cases from the Registry of Bone Sarcoma (Cases No. 154 and 291). He discussed the features in detail and defended the use of the term angioendothelioma of bone as a distinct clinical and pathological entity. Since Kolodny's contribution, cases have been reported by Pritchard (1931), Barry (1932), Warner and Singleton (1933), Brallford (1934) and Lutz and Pusch (1939). Some of these cases are registered with the Registry of Bone Sarcoma and are included in this study (B.S.R. Nos. 154, 291, 1040, 2156).

True angiosarcoma of bone is probably a rare tumor as only a few cases have been reported in the literature. There is much confusion concerning the use of the term, and many of the earlier cases were no doubt vascular sarcomas and not true malignant angiomata. Freilich and Coe in 1936 published a case of angiosarcoma of the scapula and reviewed all cases previously included in the literature. In addition to their own they listed 3 cases involving bone: one of the ribs (70), one of the femur (67) and one of the clavicle (48). Pulvertaft in 1938 reported a malignant vascular tumor of the sacrum which he called a hemangioblastoma, classifying it with Kolodny's angioendothelioma of bone. The photomicrographs accompanying the report show a degree of blood vessel proliferation more characteristic of angiosarcoma. Delitch in 1939 described a case of primary angioma of the tarsal and metatarsal bones with sarcomatous degeneration. The histological description and drawings strongly suggest that this case can be classified as an angiosarcoma. There is also a case of angiosarcoma of the os calcis reported

Clinical symptoms The clinical signs manifested by benign angioma of bone are variable and not pathognomonic. Many tumors are symptomless or produce symptoms secondarily by pressure and growth. In the vertebrae the tumor often produces pressure on the cord with neurological signs of varying degree. Vertebral angiomas associated with epidural angioma have been reported occasionally.

Roentgenographic appearance. Perlman, Bucy and Capp (10) Geschickter (23, 27) and Nemenov have called attention to certain signs appearing in the roentgenograms that are more or less characteristic and aid in the diagnosis of benign angioma. In the vertebrae the picture is characteristic and even diagnostic. There is an irregular absorption of bony trabeculae and a thickening of the remaining vertical trabeculae with resulting parallel vertical striations and loss of the normal homogeneous structure. Not uncommonly these trabeculations extend into the vertebral arches (Fig 1 a).

Involvement of the flat bones often presents a characteristic sunburst appearance in the roentgenograms (plexiform angioma). Bony trabeculations radiate from a common center usually at right angles to the plane of the bone. Cases presenting this appearance have been reported by Anspach, and Kaplan and Kanzer. Four such cases are included in this series (Fig 2 a).

The roentgenographic appearance of angioma of long bones has been described as the unique soap bubble effect. There are coarsely multifoculated areas of rarefaction which expand the shell of bone to paper like thinness, giving a cystic appearance resembling giant cell tumor. In angioma, however the loculations are somewhat smaller and within them there is a fine fibrillary framework. The cortex usually is not expanded as in giant cell tumor or bone cyst (Fig 3 a).

These roentgenographic effects are determined largely by the bone involved and rapidity of the growth of the tumor. However the roentgenogram is not always characteristic or diagnostic.

Pathological findings Bucy (9) described the histological structure of benign angioma of bone in considerable detail. With the ex-

ception of one case in this series the tumors are cavernous in type composed of large endothelium lined spaces filled with blood (Figs 1 b 2 b). The remaining case can be classified as a capillary angioma (Case No. 849). In none of the cases is there evidence of unusual endothelial proliferation, and mitotic figures are not found. The stroma is loose fibrous connective tissue and is variable in amount. Bone destruction takes place as the result of reaction to growth and not to invasion by the tumor mass. Calcification is present in one case (B.S.R. No. 1882).

Treatment and results The majority of cures in this series have been treated quite successfully by irradiation or operation or by both. Wherever possible, as in the cranium or bones of the extremities, resection or curettage and cauterization have proved satisfactory. The danger of severe hemorrhage from operation must be considered, especially in operations on the cranium and spine. In one case (B.S.R. No. 662) death occurred as a result of shock and hemorrhage following removal of the growth in the cranium.

Kranzner and associates attributed the high mortality in laminectomy to overenthusiastic surgical efforts. They warned against opening the dura or attempting to remove more of the tumor mass than is necessary to relieve pressure. They also pointed out that although high voltage roentgen ray therapy is recommended as a postoperative measure, it would seem inadequate and hazardous to use it alone when there is compression myelitis. Irreparable damage to the cord may occur before any beneficial effect can be anticipated.

Meyerdling found angioma of bone to be somewhat radiosensitive and under moderate dosage, repeated at regular intervals for a number of months, it gradually regresses until healed. In several of the cases reported by Geschickter and Copeland (23) cures were obtained by curettage followed by chemical or thermal cauterization. With these methods of treatment the prognosis is excellent, and amputation should rarely be necessary.

MALIGNANT ANGIOMA (TABLE II)

The histological variations evident in a study of malignant angiomas suggest that



Fig 1 a, Benign angioma of the second lumbar vertebra. The vertical striation is diagnostic. b, Cavernous

angioma of vertebra (B S R No 940). The blood filled channels between the bone trabeculae are very large.

they might be divided, as previously stated, into two groups, the angioendothelioma and the angiosarcoma. It must be appreciated that such a division cannot be too rigidly applied. It is very difficult or occasionally even impossible to determine into which of the two groups some of the cases should be placed. This difficulty is evidenced by the wide difference of opinions expressed by the pathologists who examined these cases for the Registry of Bone Sarcoma. Because of these difficulties in classification, all angioblastic tumors in this group are tabulated under the general heading of malignant angioma. Wherever possible, an attempt is made to indicate whether or not the tumor is considered an angioendothelioma or an angiosarcoma (Table II).

There are 15 cases in this group of malignant angioma. The sexes are almost equally represented, 7 females and 8 males. The age limits are younger than in the benign angiomas, ranging from 3 to 53 years, the majority being in the second and third decades. The long bones are the most frequently involved, although in 3 cases the tumor is primary in the bones of the hands and feet, and in 1 instance in the ileum. Multiple lesions are present in 6 cases, the multiplicity being a part of a widespread metastasis in 3. It is impossible, therefore, to ascertain accurately which is the primary lesion in some of these multiple cases.

Amputation was performed in 9 cases with apparent cure in 4, and 1 has been too recent to express an opinion. Exploration and cu-

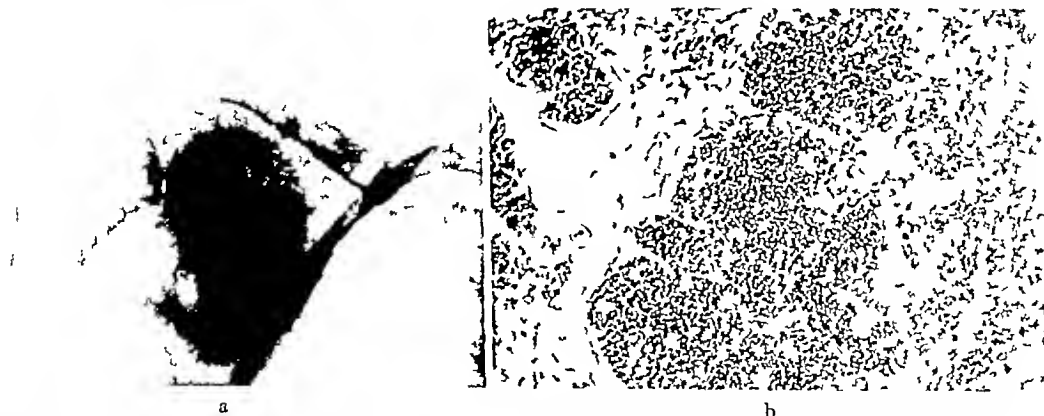


Fig 2 a, Benign angioma of scapula (B S R No 941). The "sunburst" appearance is diagnostic. b, The large

endothelial lined venous sinuses lie between bone trabeculae. Amount of connective tissue framework is small.

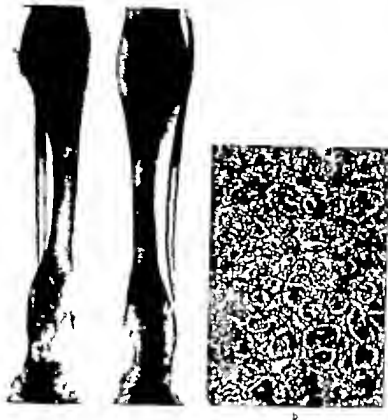


Fig. 3. a, Multiple angioma of tibia and tarsus (B.S.R. No. 35). Eosinophilic appearance with multifocal rarefaction of both the proximal and distal ends of the tibia is present. The tarsal bones present cystic appearance. b, The vascular spaces are numerous and closely packed with very slight amount of connective tissue stroma.

retirement were carried out in one case with no recurrence after 10 years. Ten patients were treated by radiation, death occurring in 6. In the 4 surviving patients treated by radiation amputation was done in all 4. In 1 case an apparent cure was brought about in the primary lesion but the tumor recurred in an adjoining bone 5 years later and amputation was necessary.

Death following metastases to viscera and other bones occurred in 8 cases. In 1 case death resulted from intercurrent disease 6 months after amputation.

Angioendothelioma. Kolodny stated that most pathologists hesitate to admit that an angioendothelioma of bone is a pathological entity. He pointed out the reasons why this tumor should be considered an entity and

defined the term as "a malignant tumor of the vascular system of bone with a typical microscopic structure and a definite origin from the endothelial lining of the vessel wall. However, be stressed that in every case of suspected angioendothelioma, the possibility of a metastatic origin must be considered and eliminated."

The histological appearance of these tumors as described by Kolodny resembles an adenomatous growth with the tumor cells arranged in alveoli and tubules. The tumor cells are large polyhedral, or sometimes cylindrical in shape with well defined cell membrane and pale vacuolar nuclei and minute nucleoli. The alveoli have a lumen sometimes filled with blood.

Hirsch and Ryerson, in a study of bone metastases from primary carcinoma of the lung

TABLE II—MALIGNANT ANGIOMAS OF BONE

No	Registry of bone sarcoma No	Sex	Age	Single or multiple	Primary bone involved	Classification	Treatment	Results	Metastasis	Necropsy
1	83	F	13	S	Humerus	Angioendothelioma	Curettement	No recurrence 10 yrs	None	—
2	154	F	10	S	Tibia	Angioendothelioma	Amputation	Died 4 1/2 yrs	Chest and skull	No
3	291	F	45	M	Entire skeleton	Angioendothelioma	Radiation	Died 8 mos	Viscera	Yes
4	798	M	17	S	Femur	Angioendothelioma	Radiation amputation	Died 2 yrs	Viscera	No
5	1007	M	47	M	Tarsus	Angioendothelioma	Radiation amputation	Died 2 yrs	Bone and viscera	Yes
6	1040	M	30	M	Radius and carpus	Angiosarcoma	Radiation amputation	No recurrence 10 yrs	None	—
7	1174	F	38	S	Femur	Angiosarcoma	Radiation amputation	No recurrence 3 yrs	None	—
8	1428	F	24	S	Fibula	Angiosarcoma	Excision, radiation	Died 4 yrs	Lungs	No
9	1482	M	30	M	Rib?	Angiosarcoma	Radiation	Died 5 yrs	Bone and viscera	Yes
10	1530	F	48	M	Femur	Angiosarcoma	None	Died 7 mos	Bone and viscera	Yes
11	1972	M	?	S	Metatarsal	Angiosarcoma	Radiation amputation	Died 2 yrs	Lungs	No
12	2126	M	38	S	Ileum	Angiosarcoma	Exploration	Alive after 1 yr	None	—
13	2156	F	53	S	Humerus	Angioendothelioma	Radiation amputation	No recurrence Died of heart failure 6 mos	None	No
14	192	M	50	S	Tibia	Angiosarcoma	Amputation	No recurrence 3 mo	None	—
15	Author's case	M	3	M	Tarsus	Angiosarcoma	Curettement radiation amputation	No recurrence 13 yrs	None	—

reviewed the problem of so called multiple endotheliomas of bones. They were inclined to cast doubt on the correctness of many such reported cases. In their opinion the assumption of multiple primary foci in bone as an explanation of coincident tumors in various parts of the skeleton seems to be due to the failure of finding a small primary carcinoma on postmortem examination or to inability to distinguish the primary group from the secondary in the presence of many tumors in different tissues. As a solution to the problem, they urged careful and thorough postmortem examination supplemented by a thoughtful interpretation of the changes thereby demonstrated.

Geschickter and Copeland (23) did not mention angioendothelioma of bone as a clinical entity in their monograph of bone tumors. Furthermore Geschickter and Masseritz (26) in a study of Lwing's tumor stated that in the

series they did not see a case of bone tumor in which the diagnosis of angioendothelioma was justified. They said it is readily understood how metastatic hypernephroma, anaplastic and mucoid forms of carcinoma, and angiosarcoma can possibly be diagnosed as angioendothelioma. Yet, in the discussion of a case of angioendothelioma reported by Lutz and Pusch in 1939, Geschickter (22) made this significant statement:

"A few years ago it would have been embarrassing to open this discussion because I was convinced there wasn't any such thing in bone as angioendothelioma, but today we have to admit that all forms of pathologic involvement of the bone of a neoplastic character have not been described. The only objection to the term endothelioma is that it is so widely misused. My conception is that these tumors arise from primitive mesoderm around joints and may be found in bone. They are not metastatic, they are moderately radiosensitive but not radio-curable and these patients should have the benefit of radical surgery."



FIG. 4. a, Angioendothelioma of humerus (B.S.R. No. 50). A large cyst-like expansion of the shaft with numerous thin, dark trabeculae and thinning of the cortex is evident. b, Gross specimen split longitudinally.

The pale tissue composing the bulk of the tumor is necrotic. The large, clear cells with eccentric nuclei are arranged in sheets, some of which are brown and rich blood.

The loose manner in which the term angioendothelioma has been used by some authorities only adds to the confusion of identifying this controversial tumor. Some use it simply as a descriptive term indicating a certain histological structure, with others it designates a definite pathological and clinical entity. Connor, for example, employs the term to describe an unusually vascular type of diffuse endothelioma (Ewing's tumor). Kolodny, on the other hand, indicates a definite clinical entity quite different from Ewing's tumor. Many pathologists today do not accept Ewing's tumor as a true endothelioma of vascular origin, but believe it to be a neoplasm originating from the reticulum or the lymphoid cells. Ewing (6, 7), on the other hand, recognizes a definite anaplastic tendency in this tumor and considers it to be a form of capillary angiosarcoma or endothelioma arising from the blood vessels of bone marrow. He classifies Ewing's tumor therefore as a form of malignant angioma. He reserves the term angioendothelioma to designate a more vascular type of endothelioma, which he describes as a solitary, cystic tumor usually developing in the ends or shafts of the long bones. The tumor presents

cords or pseudocavities and enclosing freely circulating blood. The cells are large with clear cytoplasm, sharp cell membrane and small nuclei. He further states that a similar structure may be seen in liposarcoma or in metastatic carcinoma of kidney or adrenal, which tumors must be excluded before the diagnosis of angioendothelioma can be established.

Ross wrote at length on the histological differentiation between primary bone endothelioma and hypernephroma. He believed that the two can be distinguished by a purely morphological analysis, emphasizing the importance of the relationship of the tumor cells to the surrounding connective tissue stroma in differentiating the two. In endothelioma they are intimately related to the underlying struc-



Fig 5 a, Angiosarcoma of femur with metastasis (B S R No 1530) The primary lesion is a large rarefied area just above the condyles which has broken through the cortex anteriorly The small discrete, oval lesions in the midshaft are probably metastatic b, Metastatic lesions

in the ribs are seen c, The lesion is composed of irregularly arranged vascular spaces lined by large endothelial cells and surrounded by a fibrillar network containing large numbers of similar cells Mitotic figures are seen New blood vessels evident in the section are characteristic of this tumor

of bone exists as a pathological and clinical entity is still a controversial one, although the evidence suggests that such a tumor of bone does occur The problem of diagnosis is especially difficult when the skeletal lesions are multiple, since it is often difficult or impossible to ascertain which is the primary focus In such cases metastatic lesions from a primary carcinoma or hypernephroma cannot be ruled out absolutely without a complete and careful postmortem examination In single lesions the problem is not so difficult If the patient remains well for several years following amputation or excision, it is presumptive evidence that the lesion is primary in bone

Six cases in this group of malignant angiosarcomas have been designated angioendotheliomas, although the diagnosis in some of them might be open to question because of the difficulty in distinguishing them histologically from metastatic carcinoma or hypernephroma Postmortem examination was done in 3 of the cases, however, and no evidence of primary carcinoma was found Metastasis and death occurred in 4 of the 6 cases In the 2 cases

that were not fatal, the proximal half of the humeral shaft was involved in both One of these (B S R No 83) was treated by curettage and cauterization with no recurrence 10 years later In the other case (B S R No 2156) treatment consisted of radiation and finally amputation Death occurred 6 months later from coronary occlusion but without evidence of recurrence Postmortem examination was not made

Geschickter's (22) and Ewing's (16) statement that angioendotheliomas are usually found in the ends of the long bones is confirmed by this study Examination of the roentgenograms shows a varied appearance which cannot be called characteristic or diagnostic All show rarefaction and destruction, and rarely bone production Some reveal cystic expansion with well defined septa which Brailsford described as characteristic of angioendotheliomas Such an appearance, however, is not typical of the cases in this series (Fig 4, a)

An analysis of the clinical symptoms reveals nothing significant or diagnostic The symptoms vary according to the location of the le-

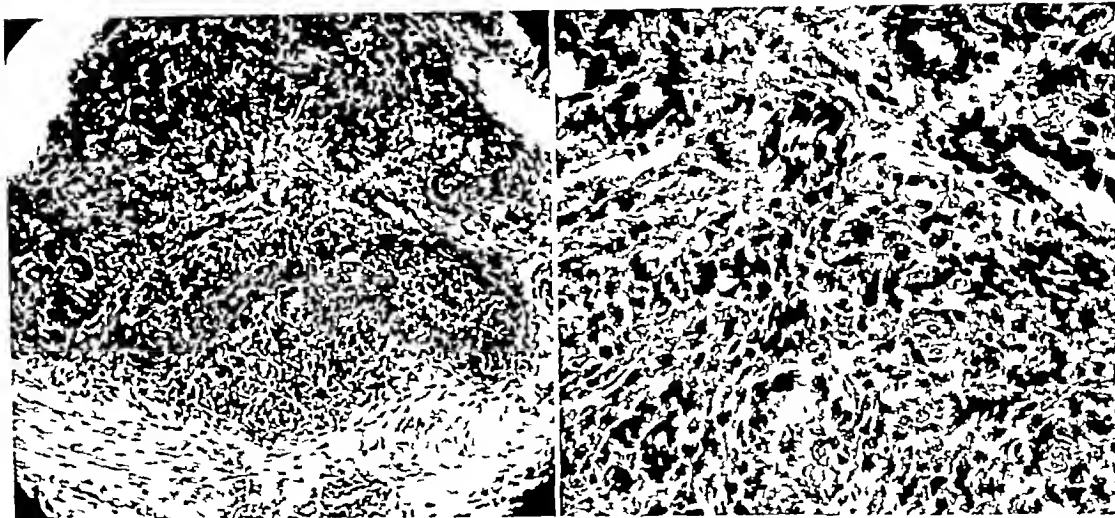


Fig 6f

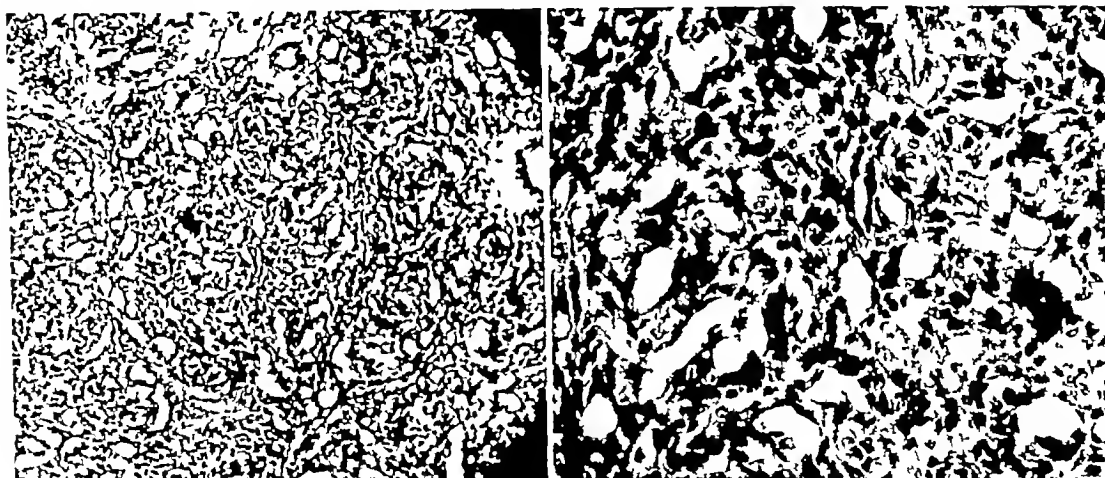


Fig 6g

matin granules. Mitoses are frequently found. The cellular areas are traversed by a varying number of wide, thin walled blood spaces which are lined by flat endothelium. In places, the blood vessels are very numerous and may even excel the strands of cells. The vessels are now less sharply differentiated from the cells surrounding them and transitions can be found between the cells in solid strands and those lining the blood spaces. Since the undifferentiated neoplastic mesenchyme reveals distinct vasoformative tendencies, the microscopic diagnosis is angiosarcoma" (Jaffe).

Telangiectatic sarcoma has been designated by some as a form of angiosarcoma, as in a case reported by Hodges, et al. In the classification

of the Registry of Bone Sarcoma, however, this tumor is placed under the osteogenic sarcomas. Ewing (17) has recently discussed its classification as follows:

"Telangiectatic sarcoma, a form of malignant bone aneurysm, is a very characteristic bone tumor, but its exact origin and relation to other bone sarcomas has not been satisfactorily determined. There is considerable evidence suggesting that this process belongs with the tumors of blood vessels of bone and is a cavernous angiosarcoma. Further data seem necessary before the true nature and relations of the so called telangiectatic bone sarcoma can be determined, and these data should relate to the part played by blood vessels in the origin and growth of

ther osteogenic sarcomas. Their clinical connections with other malignant bone tumors seem to warrant their retention, if, at present, in any complete group of bone sarcomas.

The term angiosarcoma is used in this study to indicate a malignant neoplasm showing proliferating vascular endothelium with new blood vessel formation in which the vasoformative tendency is the predominant feature (Fig. 5 a). Nine cases have been classified as angiosarcoma on the basis of this histological picture. Metastases and death occurred in 4. Amputation was performed in 5, 4 of which were alive without evidence of recurrence on last report. The author's case has been followed 13 years. Excision was done in 1 case in which the primary lesion was in the fibula, death with pulmonary metastases occurring 2 years later.

The clinical and roentgenographic signs are in no way distinctive being of little value in differentiating angiosarcoma from other malignant bone tumors. Since the diagnosis is made entirely on pathological findings biopsy is of great value.

The results in this series indicate that angiosarcoma and angioendothelioma are only moderately radiosensitive in contradistinction to Ewing's tumor. Early surgery, such as excision or amputation supplemented by radiation offers the best possibilities for cure.

REPORT OF A CASE OF ANGIOSARCOMA OF TARSAL BONES

P. S. Whit, male, aged three years, was first seen on January 9, 1926 complaining of pain in the right heel. His father stated that he limped when he first began to walk. The symptoms gradually increased in severity until he was unable to bear any weight on the affected leg. There was no history of injury.

The patient was a rather frail boy who refused to bear any weight on the right foot. Examination of the right lower extremity revealed atrophy of the thigh and calf muscles. Any attempt to move the foot caused pain localized in the medial side of the heel. There was fullness on the medial and plantar aspect of the heel. These areas were very tender to pressure, especially over the plantar surface of the heel posteriorly. The right knee was held in slight flexion, and an attempt to straighten the knee elicited pain in the foot. The physical examination was otherwise negative.

Roentgenograms (Fig. 6, b) of the right foot showed a cystic area involving the calcaneus. Inferiorly the process had broken through the cortex.

Treatment: A tentative diagnosis of tuberculosis of the calcaneus was made, and the patient was hospitalized. The foot was immobilized in a plaster of Paris cast extending from the toes to mid thigh. He was kept in bed, and heliotherapy was started. Laboratory findings were essentially negative, including the tuberculin and Wassermann tests. Instead of improving, the pain increased. It was necessary to remove the cast 3 weeks later. Examination indicated that the infiltration and swelling beneath the heel had increased, and the foot was more tender. It was therefore decided to explore the lesion by operation.

On February 20, 1926 under ether anesthesia, an aspiration was attempted without success. The calcaneus was then exposed by posterolateral flap incision. The periosteum was intact, but there was an opening in the bone cortex on the plantar surface of the calcaneus extending into a large cystic cavity. The cavity was filled with purplish red, friable tissue, resembling granulation tissue. Several small pieces of bone were lying free in the cavity. The edges of the opening were irregular and overhanging. The lesion was very vascular, bleeding freely when touched. The cavity was thoroughly curetted and then cauterized with phenol. It was necessary to pack the wound to control hemorrhage. The skin wound was loosely closed with interrupted silk worm sutures.

Convalescence was uneventful. The gauze pack was removed under gas anesthesia on the 3d day without further hemorrhage. The sutures were removed on the 10th day, the wound being apparently healed.

Pathological report: A direct smear showed organisms, and the culture was negative. Tubercle bacilli which were inoculated into three guinea pigs yielded negative postmortem findings. The microscopic examination revealed very cellular, vascular growth suggestive of sarcoma (Fig. 6, c). In view of the diagnosis, sections were submitted to two other local pathologists. Both confirmed the diagnosis. As the advisability of amputation had to be considered, slides and roentgenograms were submitted to the late Dr. Joseph C. Bloodgood, of Baltimore, who reported that he considered the microscopic appearance suggestive of sarcoma or angiosarcoma. He advised against amputation but urged continuation of the roentgen-ray treatment. Some months later photomicrographs of the tumor tissue were submitted to Dr. James E. King of New York City who expressed the opinion that it was malignant neoplasm originating from vascular endothelium, but qualified this opinion by stating that it is hazardous to draw too sharp distinctions from photomicrographs.

Progress notes: Dr. Bloodgood advised as follows, and the boy was given heavy doses of roentgen ray over the foot and leg. He was discharged from the hospital on March 30, 1926. A roentgenogram taken at that time showed increase in the

destructive process, and the edges of the cavity appeared smoother with evidence of bone condensation. He was seen at intervals for a year and a half, roentgenograms being taken frequently with no evidence of recurrence. He continued to have pain, however, and was unable to bear full weight on the affected leg.

The patient then disappeared from treatment and was not seen until 3 years later (1930) when he was readmitted to the hospital. He was walking with a crutch, complaining of severe pain in the right foot. He stated that he had not been able to bear weight on the affected leg since he was discharged. Examination revealed marked atrophy of the right lower extremity with shortening of 6 inches. There was a severe equinovalgus and cavus deformity of the foot with contracture of the plantar fascia. A roentgenogram showed that the original cavity of the calcaneus was completely healed (Fig 6, b). An attempt was made to correct the deformity of the foot by means of a wedge osteotomy. After 2 or 3 months the cast was removed, and he was discharged from the hospital.

He returned in 1933 at which time he still complained of pain and inability to walk. Examination revealed that the deformity had recurred. The foot was especially tender in the midtarsal region. Roentgenograms revealed an area of destruction involving the midtarsal bones which had not been evident in the previous pictures (Fig 6, c). In view of the new lesion and the marked disability in the leg due to pain, shortening, and deformity, amputation was performed through the middle third of the leg in September, 1933. He made an uneventful recovery and was fitted with a prosthesis 3 months later. He was last seen in November, 1935, at which time he was apparently in excellent health. Verbal reports since then indicate that he is well.

Pathological report of the amputated specimen. The foot was cut through the sagittal plane, the calcaneus and midtarsal bones being split. A dark, chocolate brown, circumscribed tumor consisting of soft, friable, very vascular tissue was found involving the navicular, cuboid, and second cuneiform bones. The calcaneus was small and atrophic, but there was no evidence of tumor tissue (Fig 6, c). Microscopically the tumor was composed of many vascular spaces lined with endothelial cells. The true angiomatous character of the tumor was much more readily discernible than in the sections from the calcaneus made 7 years previously. The blood spaces were much larger, the tumor cells being less densely packed and apparently not as proliferative as in the previous sections. Connective tissue was less dense but more abundant. Red blood cells were seen in some of the vascular spaces. Granules of blood pigment were present. Endothelial proliferation and new blood vessel formation were a prominent part of the picture. In some areas the endothelial proliferation was marked, cells being so densely packed that obliteration of vascular spaces was noted (Fig 6, g).

This case is of unusual interest not only because of its rarity in regard to type, location, and age, but also because of the rather striking changes that were observed over a period of 7 years before amputation was done. At first the tumor showed many signs of malignancy, and there was some difference of opinion among the pathologists on this point. The original sections showed such marked endothelial proliferation that the vascular spaces were almost obscured and the histological, as well as the roentgenographic, appearance strongly suggested sarcoma. As time passed, however, the primary lesion eventually was obliterated, as indicated by the roentgenograms and the pathological examination of the amputated foot. The marked shortening of the leg with atrophy probably should be attributed to the effect of the roentgen-ray therapy on the epiphyseal cartilage.

The final roentgenograms taken 7 years after the first operation revealed a surprising condition in the presence of a large destructive lesion in the midtarsal region, which had not been evident in the previous pictures. Pathological examination revealed an angiomatous tumor in this area which histologically resembled more nearly a benign capillary angioma than an angiosarcoma, although there were areas which still showed marked endothelial proliferation. Nevertheless, the structural differences between the original lesion in the calcaneus and those of the tumor in the midtarsal region were quite evident. The question arises whether the latter tumor was the result of direct invasion from the original lesion, or whether it developed from a second congenital focus, independent of the primary lesion. The serial roentgenograms and the gross appearance of this tumor suggest that the latter mode of origin was quite possible.

Because of its angioblastic tendency and its recurrence after apparent cure, this tumor is classified as an angiosarcoma of low grade malignancy. Its varied histogenesis demonstrates the difficulties involved in the identification and classification of angioblastic tumors.

CONCLUSIONS

A review of current opinions on the pathology of vascular tumors indicates that they are

mesenchymal tumors arising from congenital rests by a process of endothelial proliferation and differentiation into new blood vessels. They occur in both benign and malignant forms. They are true endotheliomas.

The typical benign angioma is a highly differentiated structure composed of fully developed blood vessels which grows slowly and with little evidence of cellular activity.

Malignant angiomas, on the other hand are characterized by rapid growth, invasion of surrounding tissue, and sometimes metastasis. They consist of very cellular angioblastic tissue which in its histogenesis tends to revert to the original primitive mesenchymal structure, producing a varied histological picture differing greatly from the well differentiated benign forms. Often in these malignant forms the primitive mesenchymal structure will assume morphological characteristics resembling either connective tissue (sarcoma) or epithelial tissue (carcinoma) rendering their histological diagnosis extremely difficult. They all possess one feature in common, however essential for diagnosis. There is always present an angioblastic tendency evidenced by endothelial proliferation and the formation of new blood vessels.

Tumors arising from blood vessels in bones are rare but their inclusion in a special class of bone tumors is justified on the basis of certain distinctive pathological and clinical features which they possess. A clinical and pathological study of 27 angiomas of bone has been herein reported.

The benign forms possess certain roentgenographic and pathological features which are practically diagnostic. These features have been described in considerable detail.

The malignant forms on the other hand are most varied in their structure and growth and offer more difficult problems in diagnosis. It is suggested that on the basis of histogenesis the malignant angiomas of bone can be divided into two subdivisions, the angioendothelioma and the angiosarcoma. Angioendothelioma is an angioblastic tumor but with an epithelium-like structure difficult to distinguish from metastatic carcinoma. In angiosarcoma the vasoformative tendency is a more predominant feature the new blood vessel be-

ing the unit of the tumor rather than the proliferating endothelial cell. Examples of both of these types of malignant angiomas are included in the series. These two groups vary greatly in their growth and malignant tendencies and they possess few characteristic roentgenographic or clinical features distinguishing them from other malignant tumors of bone. Diagnosis is based largely on their histological appearance. They are only moderately radiosensitive and early diagnosis and radical surgical treatment are essential for cure.

SUMMARY

1. A pathological and clinical analysis of 27 cases of benign and malignant vascular tumors involving bone is reported.

2. A résumé of current opinions on the pathology of vascular tumors is included, special attention being directed to histogenesis and classification.

3. It is suggested that malignant angiomas of bone can be divided into angioendothelioma and angiosarcoma. The distinctive features of each are given.

4. Treatment of vascular tumors of bone is outlined emphasizing the importance of early diagnosis and radical surgery in the malignant types.

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SUPPURATIVE JOINT DISEASE AND ITS RELATION TO PYOGENIC OSTEOMYELITIS

A Review of End Results of 67 Involved Joints in 57 Patients, Modern Chemotherapeutics

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INTEREST in the outcome from major joint suppuration appears to have been stimulated by World War I coincident with an awakening of interest in the long term outcome from injuries and disease incurred in that conflict. During that period the revolutionary and heroic treatment of Willemss was inaugurated only to fall into later disrepute among his civilian surgical successors. A rational treatment of the condition appears not to have been devised until the late Russell Hibbs contended that pus within a joint played the major rôle in destroying its cartilage. To lessen this potential damage, surgical drainage of the joint was deemed necessary to provide an avenue of escape for purulent materials. Phemister later demonstrated a tryptic ferment in the products of pyogenic suppuration and showed that a pyogenic exudate will dissolve cartilage *in vitro*. He was unable to demonstrate a similar ferment in tuberculous pus. This same author also established the fact that pressure in the presence of a pyogenic exudate accelerated the erosion of cartilage. Traction on a joint, which separates its articular surfaces, together with arthrotomy or other drainage, became the accepted and logical treatment. It is the only effective means of treating suppurating joints, but its exact application varies with the joint. This regimen led to preservation of motion in the largest percentage of cases, but it has been only in later years that end results of a large number of cases have become available. The historical aspects of the changing surgical viewpoint concerning the therapy of suppurative joints will not be reviewed in this place because excellent historical sum-

maries have preceded this paper. They will be found in the writings of Garrison Bick, Inge and Liebolt, and Wilensky.

The exact differentiation between the causes of joint suppuration had to await the successful routine application of bacteriological methods to this disease. However many years prior to these applications of bacteriology Wisseman (17th century) was credited with differentiating the clinical features of suppurative joint disease from the "tumor albus" of tuberculous disease of the knee. However this differentiation was not made with ease and certainty until Phemister pointed out the roentgen characters of suppurative joint disease as compared with those of tuberculous infection of the joints. In the former destruction of the cartilage and then the joint space occurred first in the contacted or "weight bearing" portions of the joint, while tuberculous pannus destroyed the noncontacted portions of the articular cartilage by growing over the joint from the peripheral nonweight bearing portions. The surface spread of tuberculous tissue is inhibited by motion and contact. From a clinical point of view the acuteness of suppurative joint disease usually prevents confusion with tuberculous joint involvement. In civilian life, the frank association of acute and chronic pyogenic osteomyelitis with the production of suppuration within the joints further aids in clinical diagnosis. The frequency of joint complications from suppurative joint disease has varied in the statistics of different authors. These are given in Table I. In general, there has apparently been a closer association of suppurating joints with pyogenic bone involvement in recent years. This apparent greater association of bone infection as a point of origin of

TABLE I — DISTRIBUTION OF PYOGENIC ARTHRITIS BY JOINTS—ACCORDING TO VARIOUS AUTHORS

	Bigard	Lewis (cited by Wilensky)	Wilensky	Blaisdell and Harmon
Hip	26.4%	21.1%	15.6%	34.3%
Knee	36%	41.1%	28.1%	38.8%
Ankle	22.6%		15.6%	6.0%
Shoulder	3.8%	16.4%	3.1%	10.0%
Elbow	1.9%	18.8%	15.6%	
Wrist	1.9%		3.1%	7.5%
Spine				
No cases	53	85	32	67

joint suppuration is accounted for by the smaller incidence of penetrating injuries in civilian practice and by the greater frequency of roentgenographic study of bone and joint disorders

From the historical aspect, recommendations for treatment have varied. Early surgical writers recommended simple incision of the joint "to evacuate the matter," noting that the joint finally became immobile as a result. During the period when amputation of the extremities was a popular surgical procedure, suppuration in the major joints was considered an indication for amputation. The modern tendency, except for the introduction of the Willems treatment, which is no longer generally practiced, has been toward conservatism. Roentgen visualization of the involved part has allowed the surgeon to direct his treatment intelligently toward discovery and concomitant treatment of bone suppuration. There have been no contributions of major importance since those of Phemister until the recent application of specific chemotherapy. Notwithstanding, the grade of treatment has steadily improved and with it the end-results. It should be brought out, though, that regardless of the diligence and persistence in surgical care, many cases will suffer ankylosis and loss of extremity length because of the extent of initial bone disease, a factor not under control of the surgeon in cases in which the infection has occurred by the bloodstream.

We have found 57 patients with suppurative joints in the records of the Guthrie Clinic

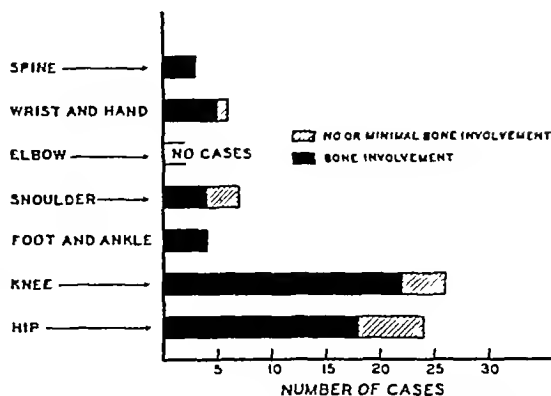


Fig. 1 Involvement of various joints by suppurative joint disease. Cross hatch areas, no or minimal bone involvement, black areas, bone involvement

and the Robert Packer Hospital. While some of these patients presented multiple joint involvement, 67 separate joints were available for study. These cases represent all those seen in a period of 8 years, but our treatment, as described in a later section of this paper, was applied to only a few of them inasmuch as it has been evolved as a result of the relatively recent applications of chemotherapy.

In general, the application of chemotherapy, following prompt diagnosis and arthrotomy, probably would result in better general outcome than that presented by this whole group of cases (Table II). Figure 1 gives the distribution of cases according to joint involvement. During the same period of time, 488 cases of pyogenic osteomyelitis were seen in this institution. Those with joint involvement made up 11.7 per cent of the total. Males comprised 70.7 per cent of this latter number, a finding in agreement with the usual greater incidence of suppurative bone disease in this group. The age incidence was 0 to 10 years, 26.3 per cent, 11 to 20 years, 29.8 per cent, 21 to 30 years, 14.0 per cent, over 30 years, 23.0 per cent. The age incidence was unknown in 7.0 per cent of the cases. The purpose of this paper is to emphasize the need for early and prompt bacteriological diagnosis by joint aspiration and vigorous and meticulous therapy including the prolonged application of traction to the involved extremity and to describe the application of specific chemotherapy both during the acute stage and as

TABLE II.—RELATIONSHIP TO BONE INVOLVEMENT AND DURATION

Name	Sex	Age at onset of joint disease	Age first seen for joint disease	Duration of active involvement	Joint involved	Previous osteomyelitis	Trans-illucent?	Result	Concomitant osteomyelitis	Status of joint six years after first
V. A.	M			19 days	L. knee		X	Cured	X	Acute
W. R.	M	7	8	5 mos.	L. hip	X	X	Healed deformity	X	Healed deformity
L. R.	M	10-11?		?	L. hip, R. hip	X		Healed deformity	X	Healed deformity
C. R.	M	62	23	6 yrs.	R. hip	X		Chronic	X	Chronic
B. R.	F	19	1	?	L. hip	?	?	Healed deformity	?	Healed deformity
H. R.	M	19	23	23	R. knee	X	X	Chronic	X	Chronic
E. C.	M	14	14	12 days	R. shoulder			Healed deformity		Healed deformity
M. C.	F	8m	8m	170 days	L. hip			Healed without deformity	X	Acute
A. C.	F			days	L. hip			Dead	X	Acute
R. C.	M	9		1 day	L. knee		X	Chronic osteomyelitis	X	Acute
B. C.	M	64	64	156 days	R. knee		X	Improved		Chronic
F. I. C.	F		24	22 days	L. knee L. shoulder			Improved	X	Acute
T. C.	M	19	46	27 days	R. hip			Cured	X	Acute
H. C.	M	13		212 days	L. hip		X	Dead	X	Chronic
W. F.	F	17		176 days	L. hip			Improved		Acute
B. F.	F	3m	3m	45 days	R. wrist	X		Cured	X	Acute
H. F.	M	14	14	276 days	R. knee	X		Cured (amputated)	X	Chronic
G. G.	M	6	6	?	Hips	X	?		X	Chronic
A. G.	F	40	43	30 days	L. knee	X		Fusion	X	Chronic
R. G.	M	8	8	40 days	R. knee		X	Cured		Acute
R. G.	M			34 days	R. knee		X	Dead	X	Acute
L. H.	F	10m	10m	19 days	L. knee		X	Cured		Acute
F. H.	M	16	15	19 days	L. hip		X	Ankylosed	X	Acute
R. H.	M	10	10	?	L. knee			Electrizing with fusion deformity	X	?
E. J.	F	63	68	14 yrs.	L. ankle		X	Unimproved	X	Chronic
R. J.	M			156 days	R. hip, L. knee		X	Cured	X	Acute
L. K.	M	23	23	18 days	L. wrist, R. hip	X		Cured	X	Acute
P. G.	F	?	35	?	L. hip	?	?	Cured	?	Chronic
M.	M	?	10		R. knee	X		Dead	X	Chronic
R. M.	M	?		?	R. knee R. hip	X		Cured	X	Chronic
A. M.	F	66	66	106 days	hip		X	Dead		fractured
R. A. N.	F	41		28 days	L. ankle	X	X	Dead	X	Chronic
J. F.	F	48	40	375	L. knee	X	X	Fusion	X	Chronic
W. P.	M	14	11	32 days	hip	X		Healed	X	Acute
T. Q.	M	10	10	recurrent	L. knee, R. knee		X		X	Acute
J. R.	M	11	11	123 days	R. knee			Healed		Acute
H. M.	M	13	16	375	R. hip		X	inches short	X	Healed
T. S.	M	14	14	3m	L. knee, R. knee	X	X	Fused	X	Acute
C. S.	M	19	10	69 days	R. shoulder		X	Ankylosed		Acute
H. S.	M	12	12	days	knee	X		Cured	X	Acute
N. S.	M	67	69	64 days	R. shoulder	X		Chronic osteomyelitis	X	Acute

TABLE II—RELATIONSHIP TO BONE INVOLVEMENT AND DURATION—Continued

Name	Sex	Age at onset of joint disease	Age first seen for joint disease	Duration of active involvement	Joint involved	Previous osteomyelitis	Traumatic?	Results	Concomitant osteomyelitis	Status of joint when seen first
L. S.	M	12	12	few days	L. ankle	\	o	Cured	\	Acute
L. S.	M	4	4	12 days	L. knee	o	\	Cured	o	Acute
F. S.	F	54	54	89 days	R. knee R. ankle	o	o	Chronic osteomyelitis	\	Acute
E. S.	F	7	15	375	R. hip	o	\	Chronic osteomyelitis	\	Subacute
F. S.	M	26	60	2	L. knee	\	o	Fused	\	Healed
G. W.	M	11d	11d	27 days	L. shoulder	o	o	Healed	\	Acute
A. W.	M	37	37	67 days	R. knee	\	o	Died	\	Acute
D. B.	M	31	37	6 yrs	L. spine	o	\	Cured	\	Chronic
B. B.	M	41	41	127 days	L. knee	o	\	Stiff knee	\	Chronic osteomyelitis
M. B.	M	31	31	365 days	L. wrist L. shoulder	o	\	Ankylosis	\	Acute
C. H.	M	35	35	23 days	R. hand	o	\	Improved	o	Acute
H. M.	M	?	?	?	L. hip	\	o	Cured	\	Healed
R. W.	M	24	24	84 days	R. hand	o	\	Amputated	\	Acute
R. K.	M	25	25	64	T 12 L-1 R. shoulder	\	o	Improved	\	Acute
D. S.	F	15	15	375 chr	R. hip	o	\	Chronic osteomyelitis	\	Acute
J. G.	M	18	18	10 days	Spine	\	o	Cured ankylosis	\	Acute

SUMMARY—57 cases

Died—7

Chronic or ankylosed or both with draining sinuses 25 improved (healed occasional minor discomfort) 5 cured (included 2 cases cured by amputation) 20

used to heal the wound. The employment of traction results in a greater percentage of movable joints in the end-results (see section on treatment)

DIAGNOSTIC CONSIDERATIONS

The patient with suppurating joint disease presents himself with a painful, swollen, and immobile joint, splinted by spasm of neighboring muscles. This situation is the sequel of either pre-existing neighboring bone disease or a penetrating local injury. Occasionally, the initial bone disease has long been quiescent and has had a recent reactivation by trauma. The usual accompanying symptoms and findings of acute or subacute infection are present fever, a variable degree of "toxemia," prostration, and an increase in circulating polymorphonuclear neutrophilic leucocytes in the peripheral blood. The local findings should immediately direct the attention of the surgeon to the joint. The chief conditions to be considered in differential diagnosis are (a)

acute rheumatic fever, (b) sympathetic sterile joint effusion produced by trauma or neighboring infection, (c) intermittent hydroarthrosis, (d) joint tuberculosis, (e) hemophilia, (f) traumatic hemarthrosis, which may accompany marginal fractures and "sprains", (g) acute rheumatoid arthritis—in children, Still's disease, (h) acute bursitis, (i) periarticular cellulitis, (j) small fractures and sprains. (See Figure 2)

In the instance of the deep lying joints—hip, shoulder, intervertebral joints and temporomandibular joints—the local joint distention may be masked by pain and muscle spasm. The presence of pus within the joint can be confirmed only by aspiration, since periarticular suppuration will often closely simulate the findings of intra-articular involvement. Aspiration is further indicated at the earliest possible moment, in order to obtain material for smear and culture by the bacteriologist. From his report, specific chemotherapy is prescribed. Aspiration is the

first step in treatment since suppurative products should not be allowed to accumulate. In certain cases this is adequately prevented by one or more joint aspirations (see section on treatment)

The surgeon should not be content with positive findings in a single joint all the joints and exposed and accessible bones should receive a meticulous physical examination since suppurative bone and joint disease is frequently multiple. The symptoms in a single joint may overshadow those in other joints and the unwary diagnostician may neglect or overlook an important part of the patient's disease. In our series, 9 patients, 15.8 per cent, presented multiple joint involvement.

The symptoms arising from the systemic phase of suppuration (septicemia) may also largely or completely mask the metastatic manifestations. In these instances, the most important consideration is the chemotherapeutic treatment of the general infection and the general care of the patient rather than local attention to the joint. Selection of the appropriate drug in these cases is essential. In addition, blood cultures should be made in every case of manifest joint disease as a control upon the adequacy of dosage of the sulfonamide series of drugs.

Roentgenograms should be made of the joint and neighboring bones when the patient is first seen. They will usually show no alterations unless the patient has had previous neighboring bone disease. The earliest finding is narrowing of the joint space (Fig. 3) which is often not detectable unless a roentgenogram of the contralateral corresponding joint is available. This narrowing is not pathognomonic of acute joint disease as it may be produced by pre-existing chronic joint disease. In the latter instance, characteristic bone markings will usually give a clue to the nature of pre-existing bone disease for example, sclerosis, osteophytes with or without bone destruction. If suppuration in the area is of recent origin, no osseous alteration

weeks after onset. The importance of these facts in relation to treatment will be brought out later. There is seldom any confusion in interpreting acute, progressive demineralization of the bones as visualized by roentgenograms taken at weekly or fortnightly intervals, for in no other condition does this process advance so rapidly. Small osseous foci which are responsible for initiating joint suppuration may not be visualized for several weeks (3-8). These smaller foci have no bearing on treatment and are of scientific interest only. See Figure 4 for representative cases of slight to moderate osteomyelitic involvement which has resulted in suppurative arthritis. In the instance of primary joint suppuration, especially if purulent products are not removed by aspiration or arthrotomy solution of the cartilage promptly occurs and a roentgenogram of the joint will subsequently show erosion of bony articular cortex or sequestration of this structure and solution of the underlying cancellous bone (Fig. 5). There is usually no need for these latter changes to occur if aspiration and prompt, adequate treatment is executed.

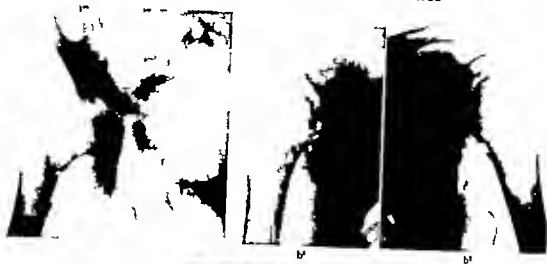
TREATMENT

Opinion is now fairly well crystallized upon the measures to be followed in treating acute and chronic suppuration within the peripheral joints. The basis for the procedures to be described has already been discussed: the indications are to preserve motion, if possible, and to relieve pain and minimize joint damage by removing suppurative products and by traction. Chemotherapy aids in controlling suppuration and in sterilizing the blood stream when involved. Some variation in treatment is needed when extensive osteomyelitis of the long bones is present, as it may not then be possible to allow joint motion to remain when appropriate treatment is being given for the extensive bone infection. The management of chronic cases differs from that in the acute stage and will be discussed



Fig 2 Roentgenograms of 5 cases illustrating different diagnosis from suppurative joint disease a, Tuberculosis of the hip in a juvenile patient. Note destruction on both sides of the joint predominating in the nonweight bearing portions of the joint b, Early tuberculosis of the knee in an adult. This case demonstrates the classical early findings in roentgenograms with marginal and intercondylar bone destruction (nonweight bearing portions of the joint) c, Hemophilic "arthritis" showing bone

atrophy, subchondral cysts, lamellation at the anterior and posterior portions of the distal femoral epiphysis and premature but symmetrical closure of epiphyseal lines d, Chondrosarcoma of the upper tibia protruding posteriorly. Bone destruction and spotty calcification in the tumor establishes the roentgen diagnosis e, Acute trauma to the knee without fracture followed by hemarthrosis. Occasionally this condition will be followed by infection when a penetrating wound is present



b^a

b^b



d

Fig. 3. Roentgenograms of suppurative arthritis involving 4 different joints in the same number of patients: a, hip; b, shoulder; c, knee; d, wrist. Note that in all these instances, there is certain amount of marginal bone demineralization adjacent and within the joint. Note also the joint sequestrum of the capital femoral epiphysis in a, b^a and b^b are taken before and after surgical removal of abscess base adjacent to the glenoid.



b

Fig. 4. Roentgenograms of small joint infections. a, Tip of acromion in an infant with infected joint infection. b, Tip of acromion in an infant with infected joint infection.

infected shoulder joint. Compare soft tissue swelling of involved shoulder with uninvolved contralateral joint. b is inferior portion of patella, ruptured into knee joint.

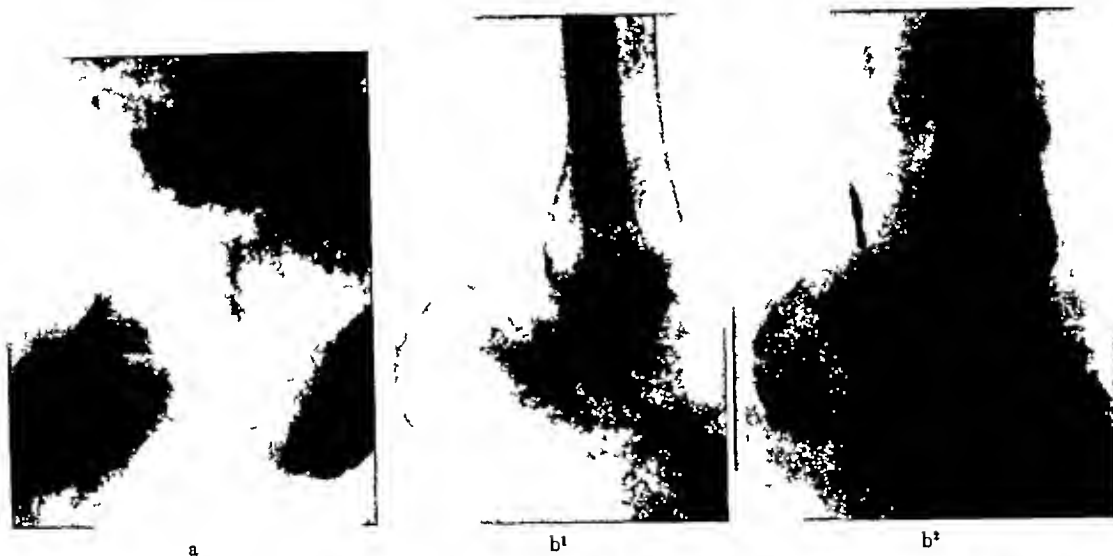
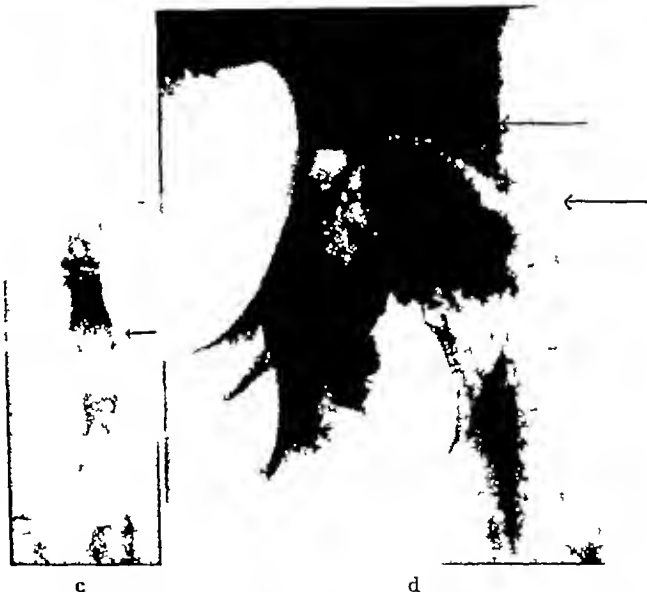


Fig 5 Roentgenograms illustrating surface erosion of bone and destruction of osseous articular cortex by suppuration a, Hematogenous osteomyelitis of the ilium in a child of 3 years, causing suppurative arthritis of the hip in which the triradiate cartilage of junction of the pelvis has been destroyed by suppuration b¹, Chronic suppurative arthritis of the tibioastragalar and the subastragalar joints in which the shadow of articular cortex on the inferior tibia and the superior and inferior astragalar surfaces has been destroyed b², The same case showing direction taken by a radio-opaque medium injected into a posterior sinus Osseous tuberculosis was ruled out in this case c, Involvement of the proximal interphalangeal joint with destruction of the osseous articular cortex d, Primary suppuration within the hip joint which has resulted in sequestration of the upper fourth of the femoral head Note loss of joint space, surface erosion of the osseous cortex over the remainder of the femoral head and subarticular demineralization in the ilium This latter was due to hyperemia neighboring a suppurative focus as demonstrated at necropsy



puncture wound, uncomplicated by osteomyelitis

CASE 1 C S, aged 4 years, was admitted to the Guthrie Clinic and the Robert Packer Hospital 8 days after a puncture wound occurred on the left foot The wound became infected and the infection ascended into the leg by the lymph channels A hypodermic needle was broken off near the patella by a local physician who first treated the patient This latter site soon became infected, the knee swelled, and walking was very painful for 2 days

just prior to admission On admission, the left knee was warm to touch, patellar ballotment associated with pain was present, and the patient was able to flex the knee but 15 degrees because of exquisite pain Roentgenograms upon admission showed the increased volume of soft tissues and the foreign body (needle) but were otherwise negative Laboratory studies were negative except for a leucocytosis—13,000—and an increased sedimentation rate—27 millimeters in 1 hour The patient was placed in bed on a Bradford frame, the left knee was extended by adhesive tape traction applied to the

TABLE III.—BLOOD AND KNEE JOINT CONCENTRATIONS OF SULFATHIAZOLE

Patient	Total (gm.) by mouth	Time after starting initial dose (days)	Blood conc. (mgm./100)	Knee conc. (mgm./100)	Pct. blood/plasma
D. R.		1 st	1 st		64
R. R.	70	30	0.3	R. L.	70 40
C. R.	30		0.8		67
M.					60
F. R.					77

grams of sulfathiazole placed in the wound when debridement and return of compound fracture of patella was performed.

leg. Aspiration of the knee joint obtained 5 cubic centimeters of purulent fluid from which the *Staphylococcus aureus* was cultured. Sulfathiazole was given the patient in 0.5 gram doses every 4 hours. In the next 3 days the temperature rose to 106 degrees F and swelling of the knee returned. Four days after admission a parapatellar rhotomy was performed, and the small foreign body was removed. Synovia was stitched to the skin in each incision and two soft rubber drains were placed through the incision, with care that neither touched cartilage. Traction and sulfathiazole were continued. On the second postoperative day the temperature did not exceed 102 degrees F and the patient appeared to have improved. He was kept recumbent in traction for more days. The rubber drains were allowed to remain in place for only 3 days until satisfactory large bilateral parapatella sinuses were established. He was discharged from the hospital, draining but little on the twenty-third postoperative day. Three days after discharge from the hospital all drainage ceased and the sinuses fully epithelialized during the following week. Six weeks after operation, almost normal range of motion was present, and the patient had no swelling or pain in the knee. On follow-up visit 7 months later the patient presented a normal appearing knee where there was a complete range of motion. Check-up roentgenograms at this time and previously failed to show an osseous focus of infection.

In this acute uncomplicated case prompt arthrotomy, aided by traction throughout the period of recumbency, resulted in a successful outcome. Previous aspiration alone did not check the accumulation of suppurative products although in 3 cases in our series repeated aspiration alone sufficed to control the infection. Sulfathiazole was used to control the hemolytic *Staphylococcus aureus* infection. In later cases healing of the sinuses has been

accelerated by the use of this drug and in some instances sulfadiazine used in a powder atomizer. This general procedure is probably applicable to the greater majority of cases of suppurative arthritis occurring in the lower extremity. Occasionally especially associated with seropurulent exudates due to infection with the α -hemolytic streptococcus, aspiration alone will relieve joint distention.

When massive acute osteomyelitis of the long bones complicates or causes joint suppuration, it is impossible to apply effective traction unless the localization of bone infection is in a site which will not interfere with its maintenance. These situations are not encountered with the frequency of uncomplicated joint suppuration and joint suppuration associated with minimal or moderate foci of osteomyelitis. The indication for cast treatment in preference to traction is the presence of pathological fracture or in the prevention of this condition. The following case of acute recrudescence of chronic osteomyelitis of the right femur with subsequent involvement of the right knee joint, is illustrative.

CASE. H. F., male, aged 26 years, was admitted to the Guthrie Clinic and Robert Parker Hospital, with a history of chronic osteomyelitis of the distal right femur of 7 years duration. The past treatment included several typical tractions and one postoperative course with maggots. He had been asymptomatic until 4 months prior to admission when he had experienced an acute local spread of the infection. Treatment had been delayed until both femoral condyles were involved by direct extension. Even at that time, involvement of the joint was not recognized elsewhere. He had had continued pain on active and passive motion due to joint involvement, even though the femoral osteomyelitis was adequately drained. Roentgen study showed diminution of the right knee joint space and painful patellar ballooning was present.

Aspiration of the knee joint controlled his pain only partially and it was not until long leg plaster was applied that he was almost pain free. The roentgen demonstration of the extent of osteomyelitis in the distal femur as a further indication for use of plaster since pathological fracture is feared.

Results that may be obtained in the future in treating these disorders may be expected to be better than the outcome in this series of cases inasmuch as the majority of these were treated before the advent of the use of the



Fig 6 Cases demonstrating contraindications to radical surgical treatment. a, left, Roentgenograms of pelvis of a child, age 10, 4 months after onset of acute suppurative arthritis of the hip and 3 months after the sequestered femoral head was removed from the draining arthrotomy wound. During this time, the patient had been in a plaster hip spica. The roentgenogram shows a bone abscess in the proximal femur with numerous small sequestra adjacent to it. b, Roentgenogram of a chronic hip joint disorder of 3 years' standing, in an adult. This was proved by biopsy and culture to be a pyogenic joint. Operative fusion was contraindicated by the supra acetabular osseous abscess.

sulfonamide group of drugs. These drugs are excreted from the blood stream into the joint in the presence of fluid exudate within these structures.

Table III summarizes cases in which the concentration of sulfathiazole in joints was determined in the presence of known blood levels of this drug. We are not cognizant of any similar observations upon record in the literature. These observations show that average concentrations of sulfathiazole in the knee joint in instances of sterile effusion are about two-thirds that of the blood concentration. Although no direct observations were made on the concentration of this drug in the instances of suppurating joints, it is likely the same or greater. At present, it is believed that there are no definite critical levels for the action of the drug, but it is desired that the blood concentration be kept between 3 and 8 milligrams per 100 cubic centimeters. To be effective in joints, however, the blood level should be kept at an adequate level which will usually result from a 4 gram initial dose

followed by 4 daily doses of 1 to 1.5 grams each in adults. Sulfathiazole or sulfadiazine will be the drugs to be used in most instances inasmuch as most suppurative joint infections are produced by the staphylococcus. It should again be emphasized that the causative bacterial organism should be determined at the earliest possible moment in order to utilize chemotherapy most advantageously.

All gradations of severity of pyogenic joint infection are encountered. The chronic types with insidious onset are rare. Their symptoms and findings are the same as those of any chronic joint disorder except pain is likely to be severe and constant. Fever may or may not be an accompaniment. A certain number of these cases are confused with tuberculous joint involvement, as the roentgen picture is likely not to be characteristic of either. Aspiration with or without joint irrigation is the only means of diagnosis. Bacterial cultures of joint contents and frozen sections of synovia establish the diagnosis when arthrotomy has been performed under the mistaken diagnosis



Fig. 7. Roentgenograms of some terminal and advanced deformities produced by suppurative arthritis (and neighboring osteomyelitis in some instances). a, End-result of wrist involvement. The proximal carpal remnants are fused to the radius. b, End result of shoulder involvement of the same patient as in a. Note the ossification in the capsule superiorly and advanced destruction of the glenoid. c and d, Flexion deformity of the knee resulting from suppuration within that joint. These films were taken years apart. Note the improvement with passive stretching and weight bearing. e, End result from pan-

arthritis of the ankle joint in which all the joints about the astragalus have been destroyed by suppuration resulting in osseous ankylosis of all bones neighboring upon the astragalus. f, Roentgenogram of knee in an adult in which slight motion had been preserved following suppuration just before this plate was taken; the patient had suffered supracondylar fracture. g, End result of suppuration within the hip which had destroyed the femoral head, portion of the neck and resulted in pathological dislocation. h, End result of suppuration within the hip resulting in bone loss and severe flexion-adduction deformity.

of tuberculosis of the joint. The infection may occasionally be sufficiently low in its virulence that bone grafts will survive when the unwary surgeon has performed an arthrodesis uncontrolled by synovial biopsy. Indications are that an increasing number of primary operations can be performed on chronic suppurating joints without the danger of sinuses developing when the sulfonamide drugs are used locally and by mouth following the operation.

The stationary case who presents himself with deformity is usually a problem involving the restoration of the weight bearing axis of the body. If the history has been that of an acute disease with rapid ankylosis with or

without drainage of the joint, the diagnosis was almost certainly that of suppurative joint disease. Before performing osteotomies for the restoration of the weight bearing axis, roentgenograms should be scrupulously inspected for the presence of small sequestra or bone abscesses (Fig. 6). In the presence of these operation should not be undertaken and should be deferred until neither are present, which may mean a period of years. There are at present, indications that the restrictions in operating upon bone formerly the seat of infection can be relaxed when local and systemic chemotherapy (sulfathiazole or sulfadiazine or both) is utilized. However the

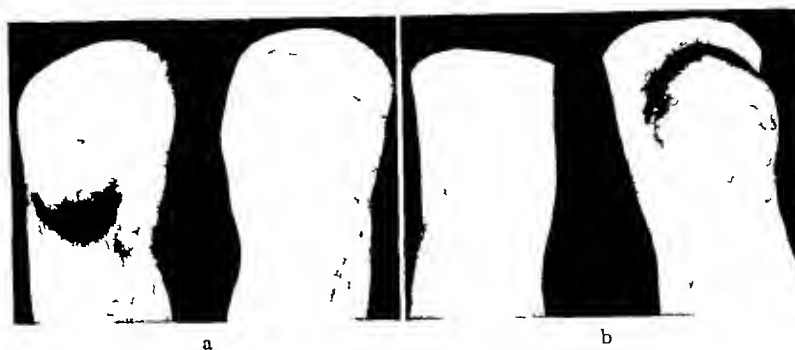


Fig 8 Two patients with prepatellar bursitis. The patient with circumscribed bursitis in, a, would less likely be confused with suppuration within the joint than the patient in, b

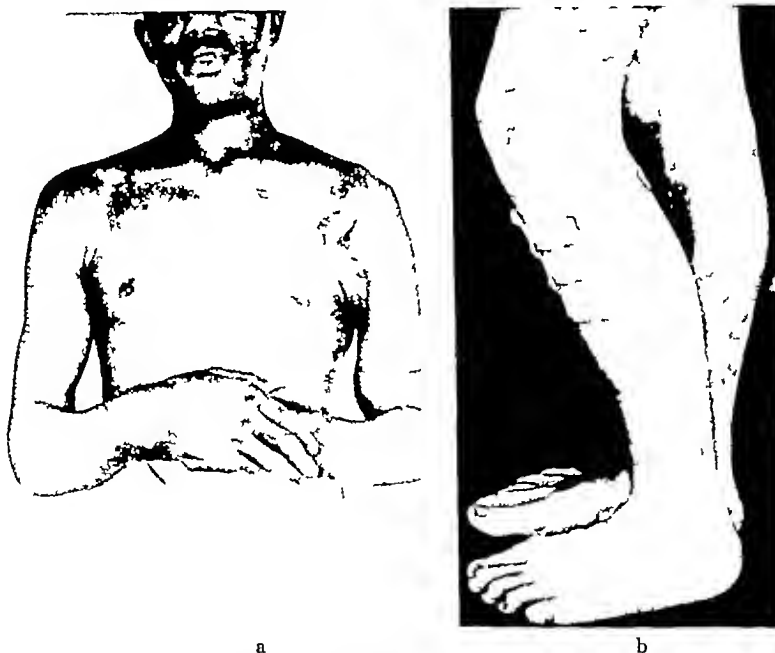


Fig 9 Two patients with residual deformity from suppurative arthritis. a, Patient 6 months after onset of suppuration in the glenoid face of the scapula. Note the loss of normal contour in the left shoulder and the drop in position of the muscle belly of the biceps due to rupture or detachment of the origin of the tendinous long head. b, Patient 4 years after suppuration in the left knee. Note flexion deformity of 30 degrees. He had only 10 degrees of motion in the knee at this time. Same patient as shown in roentgenograms, Figures 7c¹ and 7c²

limitations associated with this new auxiliary are not as yet defined and are still under clinical investigation. The factors involved in prognosis will be presented following the results in our own series of cases. Table II gives these in summary.

A review of the deformities produced by joint and adjacent bone suppuration in this series demonstrates some advanced and appalling skeletal derangements. In the acute cases, deformity was prevented by fixation in the positions of maximum function. Table II

reveals that many cases did not come under care until long periods after the acute onset. These patients, for the most part, presented deformities which under proper supervision could have been minimized or prevented entirely. Certain of these cases are illustrated in Figure 7. It is not within the scope of this paper to discuss the surgical treatment of deformities produced by suppuration within and near the joints as such a discussion would cover much of the field of reconstructive surgery.

SUMMARY AND CONCLUSIONS

1. The rationale of the treatment of acute joint suppuration by extension and arthrotomy is reviewed.

2. The outcome of 67 involved joints from 57 patients is tabulated and summarized. It is pointed out that these are poorer results than would be obtained under modern treatment with chemotherapeutic aid since the latter tends to minimize suppuration in the acute stage and to allow elective and reconstructive operations to be performed in cases in which secondary operations were contraindicated.

3. Frequency of joint involvement by suppuration is in the following order: hip, knee, ankle, shoulder, elbow and wrist.

4. The necessity of early diagnosis by joint aspiration and bacterial culture and smear is

shown, since upon the results from bacterial culture and smear the proper chemotherapeutic agent is selected. When this information is lacking during the first few hours, the chemical agents that are active against the hemolytic *Staphylococcus aureus* (sulfathiazole or sulfadiazine) are to be used presumptively and change if any made as the result of the bacteriological findings. In children who have acute joint complications following upper respiratory and middle ear infections, sulfanilamide (a hemolytic streptococci) is to be used presumptively.

5. Comparative joint and blood concentration of sulfathiazole are presented, as determined in 6 cases.

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SUPPLEMENTARY AND SYNERGISTIC ACTION OF STIMULATING DRUGS ON THE MOTILITY OF THE HUMAN COLON

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THE most uniform criticism of the drugs used to stimulate the motility of the human colon is their relative ineffectiveness in doses unaccompanied by undesirable side reactions such as nausea, vomiting, salivation, headache, and cardiovascular changes

This investigation was undertaken with the idea that a combination of drugs might be found the dose of each of which would not cause side reactions, but in combination would effectively stimulate the colon. For example, Kerr Cross found that physostigmine and pituitrin in combination had a more powerful effect on the motility of the human appendix than either drug alone, and that the use of the two drugs in combination in the treatment of postoperative distention was more effective than either drug alone

LITERATURE

Brief reference is made to some of the more recent studies regarding the action of the drugs to be used

Pituitrin A review of the literature reveals a rather wide difference of opinion in regard to the effect of pituitrin on the colon. Ochsner, Gage, and Cutting, basing their views principally on their review of the literature and observations on the dog, believe pituitrin to be ineffective. Frazier, basing his views principally on a review of the literature and on observations in man, believes that the drug is valuable in the management of adynamic ileus. He recommends that from 0.5 to 1 cubic centimeter of pitressin be given every

4 hours. According to our interpretation of the literature, pituitrin usually inhibits colon motility in the dog and usually stimulates colon motility in man. Our own experimental results confirm this interpretation.

Physostigmine The literature clearly demonstrates that this drug stimulates the motility of the canine (13, 21, 24, 29) and human (6, 9, 10, 11, 23, 24) colon. Sometimes, however, effective doses produce undesirable side reactions.

Prostigmine The use of this drug for the prevention and management of postoperative distention has been reported upon favorably by a number of authors (7, 8, 16, 17, 20, 31). Carmichael et al. observed the action of prostigmine in 41 patients. They showed that prostigmine methylsulphate in 0.5 milligram doses produces in normal subjects active movements of the colon, but there was no evidence that colon contents were moved. X-ray and barium studies revealed that considerable variation occurred in the response of different individuals to the drug. However, in the doses used, there were no side reactions and the drug was of value in gaseous distention if accompanied by an enema. The authors suggest that prostigmine followed by pituitrin and then an enema is an effective measure for stimulating peristalsis in postoperative distention. Lewis and Axelman administered prostigmine methylsulphate (1 cc 1:4000 or 0.25 mgm) as a prophylactic measure against ileus, at the time of operation and every 4 or 6 hours thereafter for 24 to 48 hours. The last injection was followed by a soapsuds enema. Prostigmine was found to be better than pituitrin. No side reactions as with eserine (physostigmine) were noted.

Ergotamine Ergotamine in large doses, apparently acts directly on the receptor mechanism

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TABLE I.—QUANTITATIVE DATA PERTAINING TO PROPULSIVE AND TOTAL MOTILITY IN THE COLON OF 4 DOGS AFTER INJECTION OF PITUITRIN, PHYSGOSTIGMINE AND PROTIGMINE

No. of experiments	Control and drug experiments	Total motility		Propulsive motility	
		per minute periods		per minute periods	
10	Controls (4 dogs)	27	61.5	64	72.5
6	salt pilocarpine	3	2.75	2.5	0
8	salt pilocarpine	20	2.5	2.5	0
17	salt pilocarpine	20	2	0	0.7
15	0.5 mgm. physostigmine	66	69	73	69
16	mgm. physostigmine	69	57.5	67.5	56
8	0.005 mgm. protigmine	4	0.7	0.6	0.1
8	C.C. 0.005 mgm. protigmine	66	26	2	0.6
8	C.C. 0.005 mgm. protigmine	73	75	67.5	59.5

Total motility in terms of per cent that the colon reacts per minute period of experimental dose. Propulsive motility calculated as per cent of total motility.

nism of muscle cells so as to prevent the cells from responding to the substance (sympathin) liberated by sympathetic or adrenergic nerve endings. In small or moderate doses the drug stimulates smooth muscle to contract for example the uterus and arterioles. Such doses are employed clinically. On this basis it was assumed that small doses of the drug might augment the activity of other stimulating drugs on the colon.

The effect of ergotamine on the motility of the intact gastrointestinal tract of man has received little attention. In doses of 1 or 2 milligrams given subcutaneously it sometimes causes nausea and vomiting (15). It delays gastric evacuation (38). Only one report (19) indicates that it may be of benefit in the management of postoperative distention.

METHODS AND PROCEDURE

Preliminary experiments were performed on dogs with an appendicostomy for the purpose of studying some of the drugs which were to be used on man. In the dog, considerable evidence is available regarding the effect of some of the drugs on *nonpropulsive* motility but none is available with direct evidence regarding their effect on *propulsive* motility.

These are the two functional types of motility found in the alimentary tract.

Experiments on the dog. Four trained dogs with appendicostomy and weighing from 19 to 36 kilograms were used. The basal colonic motor activity of each was well known as a result of previous experimentation. The colon motility was recorded by the tandem balloon technique of Templeton and Lawson. One system of two balloons was placed in the proximal colon by way of the appendicostomy. A second two balloon system, recording motility from the distal colon, was inserted through the anus to such a distance that the most caudal balloon was located approximately 6 centimeters oral to the internal anal sphincter. The balloons were connected to individual water manometers by way of T tubes and inflated according to a standard procedure (4). Since the position of the balloons is fixed, the tandem balloon method does not differentiate between propulsive and nonpropulsive motility. To differentiate such motility the propulsive force technique (4) was used. All drugs were injected intramuscularly.

Experiments on human subjects. Four ambulatory adult males with colostomy were studied by means of the balloon technique. These patients had the lower sigmoid and rectum resected from 6 to 18 months previously for carcinoma of the rectum. They were in excellent condition with no signs of metastases. The descending colon had been brought to the surface as a fistula. The subjects were under experimental observation morning and afternoon for at least 150 minutes at each session. The colon was lavaged once a day (before breakfast) and usually no material was evacuated until the next morning when lavage was again performed. During the day only slight leakage through the colostomy and normally (for them) no gastrocolic reflex which led to expulsion of material occurred.

A one or two balloon system was introduced through the fistula to such a distance that the proximal portion of the descending colon was always studied. Our observations have been made chiefly from the region near the splenic flexure. After they were inserted, the balloons were inflated according to a standard procedure (4).

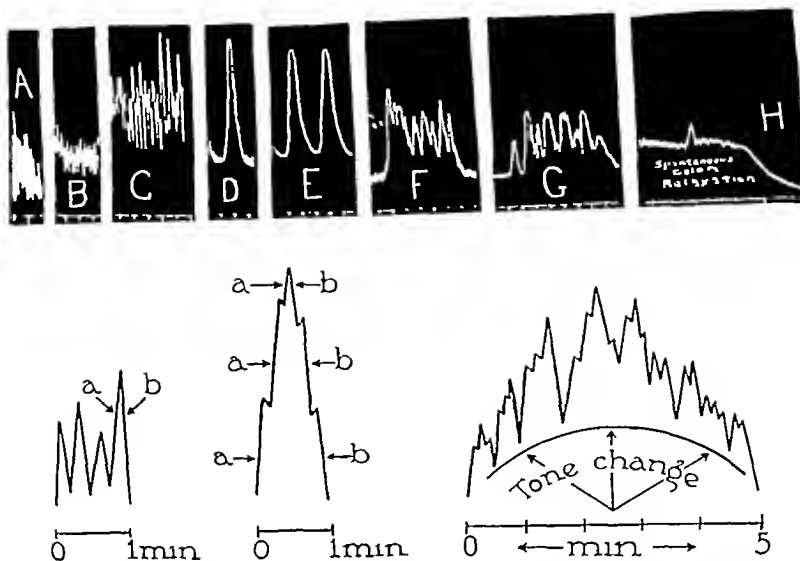


Fig 1 A to H, Excerpts of tracings from the colon of man A, B, C, type I contractions at various tonus levels, D, E, type II contractions, F, G, type III contractions, H, spontaneous relaxation of a balloon containing segment

The types of contractions are diagrammatically represented showing the manner in which complex contraction patterns are built up from more simple contractions

RESULTS

The normal or control motility *Functional types of motility* Two functional types of motility occur in the alimentary tract, one is *nonpropulsive* and the other *propulsive* in nature (28) Since drugs may affect these two types differently we have studied the effect of the drugs on each type

Types of contractions in the human colon Templeton and Lawson described three different types of contractions in the colon of the dog We have found and reported the same types of contractions in the human colon (1) and have correlated the three types with propulsion of contents Similar observations have again been made in this work and will be briefly reported at this time The types of contractions as obtained by the balloon method are illustrated in Figure 1

Type I contractions of various amplitudes, at a rate of 3 to 8 per minute occur on either high or low tone, usually on low tone They are nonpropulsive Type II contractions constitute the most frequent type of motility observed They are propulsive only when they are of large amplitude and co-ordinated with the activity of adjacent colon segments A

low amplitude type II wave may be propulsive if the contents are liquid Type III contractions consist of type II movements of variable amplitude superimposed on definite tonus waves The type III wave is a change in tonus upon which are superimposed type II contractions which may be propulsive

The quantity and functional quality of colon motility Seventy control periods of at least 150 minutes in duration were obtained from the 4 human subjects Forty similar control periods were conducted on the 4 dogs Individual variations were noted, the expulsion of colon contents was recorded as well as the nonpropulsive and propulsive motility The tracings were analyzed by adding the periods of time during which the colon was active, this gave the "total motility" The same was done for the "propulsive motility"

Referring to Table II, under the section "Experiments 2 hours after the last meal," it is to be noted that the colon of the 4 human subjects was active 53 per cent of the 50 minute period or it was active on the average 26 out of the 50 minutes of experimental time Thirteen per cent of the activity was propulsive in type, or the colon manifested pro-

propulsive motility during 6.5 minutes of the 26 minutes. When the average is taken for the 70 periods of 150 minutes each on the 4 human subjects, it is seen that motility is present 80 minutes or about 50 per cent of the time and the propulsive motility constitutes about 10 per cent of the total. In individual experiments there is sometimes considerable deviation from this average ratio. However the averages are significant because the most important analysis which can be made of the effects of drug administration on the colon is the extent to which each drug or drug combination affects the ratio of total motility to propulsive motility which normally is about 10:1. Of course the quantity and quality of motility is subject to variation in the same and different human and canine subjects. During the course of an experimental period sudden changes in tonus and motility may occur which cannot be predicted. This emphasizes the necessity of obtaining numerous control studies when drug effects are to be evaluated. The averages of a number of tests minimize the error due to such spontaneous changes. In the human colon, periods of quiescence in a given segment may endure for as long as 60 minutes. On the other hand, periods of activity 180 minutes long have been observed in a segment of distal colon. Further the activity of one segment is not an index of the type or the presence or absence of activity in a segment 3 to 4 inches proximal or distal. As in the dog at times the motility of two adjacent segments appears to be integrated or co-ordinated at other periods inco-ordinated.

The averages for the 30 control periods on the 4 dogs (Table I) and are similar to those for the human (Table II). The action of the drugs on the dog's colon will be presented first.

The action of pituitrin. Dog. In 27 experiments of 150 minutes duration (Table I) surgical pituitrin injected intravenously at a rate of 0.1 cubic centimeter per 10 seconds for 5 units or intramuscularly in 5 unit doses (0.15 to 0.25 units per kgm.) invariably inhibited motility almost immediately and often definitely decreased the tonus. This effect lasted for from 30 minutes to several hours. In 20 of the experiments (intramuscular injection) de-

pression of the motility took place in 5 to 10 minutes regardless of whether the drug was injected at a time when the colon was showing strong spontaneous motility or was in a state of quiescence. The distal colon was more profoundly depressed than the proximal, often remaining quiet for an hour after the motility in the proximal colon had returned to normal. In 2 instances it was observed that at least one balloon containing segment in the proximal colon was active whereas the remaining balloon containing segments in the proximal and distal colon were quiet.

In 12 experiments (Table I) smaller doses of pituitrin ranging from 1 to 2 units also inhibited motility but for a shorter time. Larger doses of pituitrin (10 to 15 units) sometimes had a side effect causing apprehension on the part of the animals, but the effect on the colon was the same. At no time was any stimulation of the colon motility in the unanesthetized dog seen after doses of pituitrin ranging from 1 to 15 units were injected. As one would expect, administration of pituitrin caused inhibition of balloon bolus propulsion and decreased propulsive force measurements when those techniques were employed (Table I). The results on the human colon were quite opposite (*vide infra*).

Physostigmine sulphate Dog. By trial it was determined with the 4 balloon tandem technique that 1 milligram (0.015 to 0.025 mgm. per kilogram) of physostigmine given intramuscularly to 4 dogs was effective in producing propulsive motility. Two milligrams was too powerful, causing repeated defecation in all dogs, while 0.5 milligram stimulated the colon in only 12 or 16 experiments. One milligram in 14 experiments gave no untoward side effects, and the tandem balloon system showed that the whole colon participated in the reaction. However tonus was increased and maintained at a high level in only 3 instances. Most frequently rapid tone changes appeared in the form of propulsive type II contractions which were propagated distally from the proximal to the distal colon.

Eight experiments conducted on 4 dogs using the balloon bolus technique (3, 5) showed that the bolus moved rapidly from proximal

TABLE II—QUANTITATIVE DATA PERTAINING TO PROPULSIVE AND NONPROPULSIVE MOTILITY IN THE HUMAN COLON AFTER DRUG ADMINISTRATION

Experiment	Drug and dose (mgm)	Experiments 1 hr. after last meal						Experiments 30 min. after last meal					
		Total motility			Propulsive motility			Total motility			Propulsive motility		
		5 min. periods			30 min. periods			5 min. periods			30 min. periods		
		1	2	3	1	2	3	1	2	3	1	2	3
1	Control (saline)	5	6	10	13	17.5	7.5	71	0	72	11.0	0.5	0.5
10	1 mgm. physostigmine	42	1	41	45	0	6.3	65	65	6.5	42	10.5	10.2
20	1 mgm. physostigmine	12	1	2	1	15	1.6	81	8	81.5	12	15.4	12.1
	Physostigmine (1 mgm. and 1 mgm. at 15 min.)	12	1	1	1	15	1.6	61	74	5	44	20.5	21
30	1 mgm. physostigmine (15 min.)	62	24	61.5	12	22	1	75	82	81.2	0	24.4	34.4
40	1 mgm. physostigmine (15 min.)	42	12	64	0.6	17.2	12.6	65	64.5	6.4	13.4	13.4	14.5
1	1 mgm. physostigmine (15 min.)	64	2	1	41	1	10	1	61.4	77.6	10	26	11
11	0.5 mgm. physostigmine (15 min.)	4	2	45	11	10.1	0.6	65	61.8	61.4	12	14	8.6
2	0.5 mgm. physostigmine (15 min.)	42	65	45	17.5	0.6	11.0	65	1.4	74	10.8	0.8	11
3	0.5 mgm. physostigmine (15 min.)	1	5	4	24	1	4.3	4	1	4	12.6	22	20
4	0.5 mgm. physostigmine (15 min.)	65	35.4	65.4	14.1	12.1	11.8	68	62.6	1.4	12.3	13.1	11.8
12	0.5 mgm. physostigmine (15 min.)	65	1	24	10	21	21	62	65.1	21.8	44	25	25

Total motility—measured in the three 5 min. periods (or 15 min. of experimental time).

Propulsive motility—calculated as a percent of total motility.

*Physostigmine—Serravallo's physostigmine (Parke, Davis and Co.).

†Prostigmine—Hoffmann-La Roche, Inc.

‡Prostigmine—Eli Lilly and Co. (Eli Lilly and Co. Medical Works, Inc.).

colon to distal colon after administration of 1 milligram of physostigmine. Single integrated type II contractions were capable of moving the bolus 10 to 15 centimeters in a few seconds. In only 1 case did a wave initially propel the bolus orally (reversed movement) for about 4 centimeters after which a second wave shifted it distally. Light additional experiments conducted upon the 4 dogs with the propulsive force measuring apparatus (4) showed that the colon motility following the injection of 1 milligram physostigmine intramuscularly was highly propulsive. Tracings were obtained in which the individual type II contractions registered a propulsive force equivalent to 120 grams. Such waves of propulsion were recorded for 1 to 2 hours after the initial reaction of the colon to the physostigmine occurred from 15 to 25 minutes after intramuscular injection, and endured for several hours (Table I).

Prostigmine methylsulphate. Dog. Lighten experiments conducted on 4 dogs with the use of the tandem balloon technique and the techniques used to measure propulsive motility revealed that prostigmine in doses of 1 cubic centimeter of a 1:4000 solution (0.25 mgm) gave about the same results as 0.5 milligram of physostigmine. Doses of 1 cubic centimeter of a 1:2000 solution (0.5 mgm) were much more effective and were equivalent in action to 1 milligram physostigmine. The propulsive waves were coordinated so that they were propagated to adjacent distal segments of the colon. No side effects other than increased salivation were noted with even 2 cubic centimeters of 1:2000 prostigmine methylsulphate, but motility initiated in 8 such experiments on 4 dogs resulted in defecation (Table I).

Drug actions on the colon of man. In the experiments on the human subject the blood pressure and heart rate were recorded at 5 and

then 10 minute intervals during the first hour after injection of the drugs.

Pituitrin. Man. In 31 experiments surgical pituitrin in doses of 1 to 2 units was injected intramuscularly into the 4 subjects. Within 3 minutes after injection (Figure 2 A) and in 28 instances strong co-ordinated type II contractions resulted, which were sensed by the subjects and culminated in the expulsion of material and flatus from the colostomy. The action of pituitrin in this dosage usually persisted for 15 to 20 minutes. In 2 experiments the response was slight, in 1 instance the pituitrin had no discernible effect.

As indicated in Table II the total motility during the first 50 minute period was slightly below the control level, but there was a decided increase in propulsive motility. With these small doses the blood pressure and heart rate were not changed and the subjects had no sensations other than those associated with propulsion of colon contents.

Physostigmine sulphate. Man. Twenty experiments were conducted in which physostigmine in doses of 1 or 3 milligrams were injected intramuscularly. Expulsion of colon material and flatus occurred in from 20 to 40 minutes after injection due to an increase in total and propulsive motility (Table II). With 1 milligram the results were variable in the different subjects. One patient was nauseated on 3 occasions, and vomited during one period 2 hours after injection. The colon of a second patient showed no reaction to the injection of 1 milligram of physostigmine and he manifested no side effects. On other occasions he was given 1 to 3 milligram injections and both the propulsive and nonpropulsive motilities were decidedly increased. Heart rate and blood pressure were not changed with these doses nor did he have sensations other than those resulting from increased colon motility.

If the dose of physostigmine is sufficient to initiate colon motility the stimulation may persist for several hours after injection (Table II). When the doses were graded for each subject, physostigmine acted on the colon without producing side reactions. However no correlation was found between the weight of the patient and his tolerance to physostigmine. Furthermore the reaction of the colon

to 1 milligram of the drug varied in the same individual on different occasions. Therefore, an accurate correlation between these dosages and effect on colon motility was not evident.

Simultaneous injection of pituitrin and physostigmine sulphate. Man. In 23 experiments, 1.25 units of surgical pituitrin plus 0.7 to 1 milligram of physostigmine were injected simultaneously. Pituitrin action appeared within a few minutes and endured for about 20 minutes. Following the action the physostigmine effect became manifest and lasted for several hours. It seems significant that whereas 1 milligram of physostigmine used alone failed to produce a good motor effect in this one patient referred to previously on 3 of 6 occasions a good motor reaction resulted from the physostigmine when combined with pituitrin. The second patient who was nauseated by 1 milligram of physostigmine manifested a good motor response without nausea to 0.7 milligram plus 1.25 units of pituitrin. In the 2 remaining patients no definite evidence of synergistic action of the 2 drugs was obtained but there was no doubt regarding the supplementary effects of the 2 drugs.

With physostigmine alone in adequate dosage, especially with the combination of pituitrin and physostigmine, facilitation of the gastrocolic reflex to a meal ingested 2.5 hours after injection was almost uniformly observed.

Prostigmine methylsulphate. Man. Prostigmine methylsulphate in doses of 1 cubic centimeter of a 1:1000 solution (0.25 mgm.) and 1 cubic centimeter of a 1:2000 solution (0.5 mgm.) was given intramuscularly in 30 experiments of 150 minutes duration (Table II). Twelve of these experiments on 4 subjects using the 0.25 milligram dose resulted in augmented motility in 7 instances. There was an increase in both the total and propulsive motility. With this dose, however the time of onset of action was variable. The shortest latent period was 20 minutes and the longest 1.0 hours. Tonus during the period of observation was sometimes, but not uniformly, increased. In 3 instances the increase in total and propulsive motility was slight, and in 1 there was no apparent effect. The latter 2 and 1 of the former 3 occurred in same patient who was not affected by 1 milligram physostigmine.

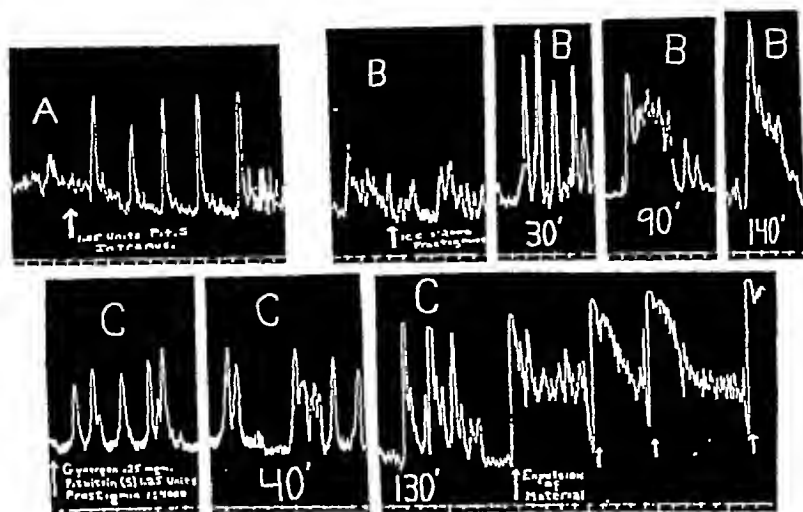


Fig 2 A, Propulsive motility in the colon of man initiated by 1.25 units surgical pituitrin injected intramuscularly, B, propulsive and nonpropulsive motility in the colon of man after intramuscular injection of 1 cubic centimeter of prostigmine 1:2000 (0.5 mgm), C, motility after simultaneous intramuscular injection of gynergen (ergotamine tartrate 0.25 mgm), surgical pituitrin (1.25 units), and 1 cubic centimeter prostigmine 1:4000 (0.25 mgm). The last 4 arrows indicate expulsion of material from the colon.

Eighteen injections of prostigmine methylsulphate (0.5 mgm) were made in the 4 subjects. In all cases there was a definite increase in propulsive and total motility (Figure 2, B) for several hours (Table II). However, as with the smaller dose there was variation in the time of onset of motility. The shortest latent period was 12 minutes and the longest 80 minutes. Facilitation of the gastrocolic reflex was definite in 14 of the experiments. There were no side reactions or definite changes in heart rate and blood pressure encountered in any experiment with prostigmine methylsulphate in these dosages. One cubic centimeter of prostigmine 1:4000 (0.25 mgm) was found to be about as effective in activating the colon segments as 0.5 milligram of physostigmine sulphate, while 0.5 milligram of prostigmine was equivalent to 1 milligram of physostigmine in 3 patients and apparently better in 1.

Prostigmine bromide tablets (15 mgm). *Man.* One tablet containing 15 milligrams of prostigmine bromide was administered by mouth in 16 experiments. During the experimental time (3 hours) the drug in 11 instances produced no decided action (Table II). On 5

occasions the action appeared about 2 hours after administration, as evidenced by an increase of total and propulsive motility with expulsion of material. These facts do not indicate that the drug is not effective by mouth because in all cases except one, the subjects reported the repeated evacuation of colon contents when they were at home. This action appeared during a period 5 to 8 hours after the tablet was given, and a decided increase in this effect followed ingestion of a meal.

Prostigmine methylsulphate (0.25 mgm) plus pituitrin (1.25 units). *Man.* In all of 16 experiments, the combination of 0.25 milligram of prostigmine methylsulphate and 1.25 units of pituitrin injected intramuscularly caused an increase in total and propulsive motility and resulted in the expulsion of colon material and flatus. The expulsion of material occurred within a few minutes and continued for several hours, the initial response being due to the pituitrin and the continued response to prostigmine. As in the experiments in which pituitrin was combined with physostigmine, it was difficult to be certain of synergistic action, since each drug is individ-

ually effective. However in all cases the action of prostigmine (0.25 mgm.) seemed to be more effective in expelling colon contents when combined with pituitrin than in those experiments in which it was injected alone. No side reactions or changes in blood pressure or heart rate were noted with this combination.

Ergotamine tartrate solution and tablets (Gynergen) Man In 12 experiments ergotamine tartrate was injected in doses of 0.25 milligram, with no discernible effect on the colon. In 6 additional experiments 1 tablet of gynergen (1 mgm.) was given by mouth. Our motility records showed no deviation from normal expectancy, nor were latent actions on colon reported by patients. With these dosages no side reactions occurred.

In 14 experiments on the dog it was found that 0.35 milligram of ergotamine tartrate (0.0097 to 0.0184 mgm per kilogram) given intramuscularly caused an increase in both the propulsive and nonpropulsive motility. In 7 instances the increased motor activity culminated in defecation. However the human subjects varied from 63 to 86 kilograms therefore on the basis of body weight the dogs received 4 to 6 times as much ergotamine.

Ergotamine tartrate (0.25 mgm) plus prostigmine methylsulphate (0.25 mgm) Man As indicated above ergotamine in 0.25 milligram doses injected intramuscularly had no action on the motility of the colon. However when this dosage of ergotamine was combined with 0.25 milligram prostigmine methylsulphate in all of 12 experiments a potentiation of the prostigmine action resulted. The motility initiated by this combination was even more propulsive than that resulting from 0.5 milligram prostigmine (1 c.c. of 1:2000 solution) when used alone. Motility appeared on an average much sooner (18 min.) and apparently had an increased capacity to move colon contents. The total quantity of motility initiated was about the same as that observed after prostigmine (0.5 mgm.), but the propulsive motility was somewhat increased (Table II). This propulsive motility was very powerful. On two occasions the most proximal balloon was tied into a simple knot even though the tube and balloon were reinforced by a flexible steel spring. Facilitation of the gastrocolic

reflex to a meal ingested several hours later was definite in all 4 subjects.

In 8 additional experiments, after a control period of 30 minutes, 1 tablet of ergotamine tartrate (1 mgm.) was given simultaneously with 1 tablet of prostigmine bromide (15 mgm.) In an average time of about 90 minutes the action of the prostigmine bromide became evident. Although the effect of the drugs together did not last longer than the prostigmine bromide alone, the response was more marked and was associated with repeated expulsion of fecal material and flatus.

Five of the experiments were conducted during the morning session and facilitation of the gastrocolic reflex to lunch was evident. An increased motility during the afternoon session was graphically recorded. Both the nonpropulsive and propulsive motilities were increased. The 3 remaining experiments of this series were conducted in the afternoon. The patients however reported facilitation of the gastrocolic reflex to their dinners 6 hours later as indicated by repeated evacuations of colon contents.

Simultaneous administration of prostigmine methylsulphate, pituitrin and ergotamine tartrate. Man. Table II presents the results of 12 experiments in which a combination of ergotamine tartrate (0.25 mgm.) prostigmine methylsulphate (0.25 mgm.) and pituitrin (125 units) was injected simultaneously. An increase in both total motility and propulsive motility resulted, the latter being very definitely increased and causing the expulsion of colon contents. The enhanced motility was evident within a few minutes, due to the pituitrin action and endured for several hours due to the marked synergistic action of the ergotamine and prostigmine. Only 12 experiments were conducted because of the potency of the mixture. On 3 occasions the proximal balloon was tied into a simple knot. This occurred immediately after very strong type II propulsive waves which caused expulsion of colon contents and sometimes the balloon and tube (Figure 3 C).

Most important is the fact that this strong action on the colon was not accompanied by side effects. The subjects felt well, with no significant changes in pulse rate or blood pressure.

EVALUATION

The importance of distinguishing between the two functional types of motility, propulsive and nonpropulsive, is confirmed by certain observations presented in this as well as in previous papers (1, 3, 4). For example, it has been shown that morphine sulphate (16 mgm) increases the total motility and tonus of the distal colon and the ileum of man (2). However, the increase in total motility is the result of an increase in motility of the non-propulsive type, the propulsive motility and discharge of colon contents is markedly decreased. In the present work if we had given attention only to the recording of total motility we should have concluded that pituitrin decreased or had little effect on the motility of the colon. The records of propulsive motility, however, showed that propulsive motility and discharge of contents from the colostomy were increased for a short period after injection of a small quantity of pituitrin. Physostigmine sulphate and prostigmine methylsulphate are examples of drugs which stimulate both functional types of motility. Thus we have examples of 3 types of drug action on the colon: *one exemplified by morphine in which the chief effect is an increase in nonpropulsive and a decrease in propulsive motility, a second exemplified by pituitrin in which the chief effect is an increase in propulsive motility with little or no increase in the nonpropulsive, and a third exemplified by prostigmine in which both types of motility are increased.*

The importance of using, at least in some experiments, a tandem balloon system in studying drug action on the colon is confirmed by observations made in this work. In a previous study it was observed that effective propulsive motility (the transportation of contents) is dependent upon the existence of co-ordination between adjacent segments. That is, if distal adjacent segments of the colon manifest high tonus, or types of motility not conducive to co-ordination of activity, the appearance of a propulsive wave in a proximal (oral) segment will not be propagated onto the adjacent distal segment to effect transportation of colon contents. In such instances, if the propulsive wave in the proximal segment is high grade and does not "pass

onto" the distal segment, the patient reports a "cramp-like sensation." This has been referred to as dyskinesia. In a number of instances dyskinesia was observed and a "cramp-like" sensation was reported after 1 milligram of physostigmine. No contents were passed from the colostomy. Contents were present in the colon, since later a wave of no greater amplitude than formerly would arise, be propagated to the distal segment and contents would be expelled. Any existing cramp-like sensation would then disappear.

Prostigmine methylsulphate and pituitrin in the doses used in our subjects, appeared to promote a co-ordinated type motility between segments, resulting in propulsion of contents. Propulsive waves were quite uniformly propagated and cramp-like sensations were not reported. It is entirely possible that in some subjects, depending upon the degree of dyskinesia existing between adjacent segments of the colon, the amount of gas present and the consistency of the colon contents, the same doses of the two drugs might cause cramp-like distress. It must be remembered here that our studies were made on presumably normal colons under uniform, controlled conditions.

The combination of *physostigmine sulphate with pituitrin* resulted in the addition of the effects of each. The rather prompt and transient action of pituitrin in the small dose used, was followed by the more delayed and prolonged action of physostigmine. The only evidence of synergistic action was observed in 1 patient who did not respond to 1 milligram of physostigmine alone, but did to the combination of pituitrin and physostigmine. The same was true of the *prostigmine methylsulphate with pituitrin* combination. This latter combination is to be preferred since doses of prostigmine (0.25 mgm) and pituitrin (1.25 units) which caused strong propulsive movements gave no side reactions as do similarly effective doses of physostigmine.

Ergotamine tartrate (0.25 mgm) alone had no significant effect on the motility of the colon of our subjects. When ergotamine tartrate was combined with prostigmine methylsulphate (0.25 mgm) the action of prostigmine was definitely augmented, i.e. 0.25 milligram of prostigmine was as effective as 0.5 milli-

gram given alone. Contents were still being discharged at the end of a 3 hour period of observation and the "gastrocolic" reflex was facilitated; this indicates that the propulsive motility of the small intestine was also augmented. Ergotamine tartrate and prostigmine were combined on the presumption that the ergotamine would increase the excitability of the colonic musculature by direct action and hence augment the response to prostigmine. This explanation may be too simple, but is supported by the observation that ergotamine increases the sensitivity of the intestine to distention and the initiation of peristalsis (27). From the results on the normal colon, this combination we believe should be tried clinically in cases of postoperative distention.

The most effective combination, in regard to the duration of action appeared to be ergotamine tartrate (0.25 mgm.) prostigmine methylsulphate (0.25 mgm.) and pituitrin (1.25 units). It was effective and our subjects complained that, after receiving this combination material was intermittently discharged from the colostomy for 6 to 8 hours after injection. With the combination of the 3 drugs the most powerful propulsive contractions we have recorded (Fig. 1 C) occurred. As noted before, in 3 instances these contractions tied the most orally located balloon into a simple knot. No cramp-like distress or side reactions were reported to accompany the powerful propulsive motility initiated by this combination. We believe that this combination should also be studied in adynamic ileus and megacolon since the duration of action on the colon of 4 normal subjects extended over a period of 6 to 8 hours.

The concept of functional segmental motor activity of the colon. Our observations show that the colon is composed of functional segments which cannot be described on a structural basis. Anatomically the segments of the colon are usually referred to as the ascending, transverse, descending and sigmoid colon. On the basis of motor activity the colon is composed of small or large divisions depending on the type of motility which is being manifested at any particular time. When 3 centimeters (length) balloons in series are placed 7 centimeters apart, 2 adjacent segments may

manifest different types of motility. In this sense each segment represents a functional unit. When 2 adjacent segments manifest the same general type of motor activity so that a wave conducive to propelling material is propagated from one to the other then the 2 segments represent an integrated or co-ordinated functional unit. In a "mass peristalsis" as in defecation an entire anatomic division of the colon represents a functional unit, so that occasionally a "mass peristalsis" starting in the distal transverse colon may pass over a number of segments in sequence including the rectum.

We have no information regarding the presence or absence of motility in the segments of the colon between the balloons, except when a propagated wave passes from one balloon-containing segment to another. In mass, a single haustrum or a group of adjacent haustra may represent a functional motor unit, and the balloon may record the activity of the local group of haustra. Thus, a local type II contraction may represent propulsion from, or an attempt to propel material from, one haustrum to another. The type I contractions represent the nonpropulsive activity of the haustra exposed to the balloon. The change of a type I into a segmental type II wave which is not propagated to the adjacent balloon-containing segment would indicate that some stimulus has caused the local haustra to become co-ordinated so that local propagation of a wave for a short distance can and does occur. For a mass peristalsis the co-ordination must spread in sequence from one haustrum or group of haustra to another or the original stimulus must in some way exert a widespread integrating influence, probably sequential, on the more distal segments of the colon. The rise in tone or wave-like sustained contraction manifested in the type III activity must represent a simultaneous contraction of several haustra since it is difficult to visualize how the contraction of a single haustrum could produce the observed mechanogram.

This concept of the functional segmental motor activity of the colon serves as a basis for the explanation of the normal physiological activity of the colon and readily explains the findings or results of the so called unstable or

irritable colon, which represents a dyskinesia of the colon. This concept requires that, if a drug is to be effective in adynamic ileus, it must not only increase the tone of the musculature but must also act so as to facilitate the genesis and propagation of propulsive waves from one segment to another. A drug that would only increase tone and non-propulsive motility would lead only to a churning and local pooling of the contents giving a "sausage-string" effect. Considering the duration of action and the absence of side effects, prostigmine methylsulphate is the best single drug among those studied, for the genesis and propagation of propulsive waves from one segment to another. The other drugs as pituitrin and ergotamine tartrate may be used to supplement or potentiate prostigmine methylsulphate.

SUMMARY AND CONCLUSIONS

The functional motor activity of the canine and human colon can be best described as being propulsive or nonpropulsive in character. The relation between the types of contractions recorded by the balloon method and the functional result has been outlined.

The data obtained in 70 control studies on 4 human subjects with colostomy show that the propulsive motility in the distal colon constitutes on the average about 10 per cent of the total motility. This value is similar to that obtained in 4 dogs, the average being about 13 per cent. The effects of single drugs and their combinations were analyzed for the extent of change in the 2 types of functional activity. All solutions were given intramuscularly, the tablets were given by mouth.

1 Pituitrin in the relatively small dosage of 1 to 2 units caused an increase in the propulsive motility of the human distal colon but did not on the average increase the total motility above the control. In the dosage used its action usually did not last longer than 20 minutes. The action of pituitrin on the colon of the unanesthetized, trained dog with appendicostomy was opposite to that on the human colon. Doses of 1, 2, or 5 units invariably depressed motility and sometimes tonus. This depression, depending upon the dose, was manifest for from 30 minutes to

several hours, the distal colon being more affected than the proximal.

2 In doses of 1 milligram, physostigmine sulphate increased the total and propulsive motility of the canine and human colon. It was difficult to grade the dosage so as to avoid side reactions and yet stimulate adequately the propulsive motility of the colon.

3 The simultaneous injection of 1 to 2 units of pituitrin and 0.7 to 1.0 milligram of physostigmine sulphate resulted usually in a supplementary action on the human colon. In 3 subjects the pituitrin acted first, increasing propulsive motility and was followed by physostigmine action which increased both propulsive and nonpropulsive motilities. In one subject there was an apparent synergistic action because in 3 of 6 instances 1 milligram of physostigmine when injected alone elicited no definite colon response.

4 Prostigmine methylsulphate in doses of 0.25 milligram was approximately equal in its action to 0.5 milligram of physostigmine on the motility of the human and canine colon. The 0.25 milligram dose was not effective in all experiments. When the dosage was increased to 0.5 milligram effective propulsive motility resulted in all cases. The nonpropulsive motility was also increased. No side effects were noted with either of the above dosages in dog or man.

5 Prostigmine bromide tablets (15 mgm) given orally to the 4 human subjects resulted in an increase in total and propulsive motility, during the experimental time (150 min), on only 5 occasions. In 10 experiments increased expulsion of colon material occurred 5 to 8 hours after administration. In 1 instance there was no effect.

6 The simultaneous injection of prostigmine methylsulphate (0.25 mgm) and pituitrin (1.25 units) resulted in an increase of propulsive as well as nonpropulsive motility of the human colon. The pituitrin in this dosage initiated propulsive motility which lasted for about 20 minutes, then the prostigmine action appeared and usually endured for several hours. In 1 patient synergistic action apparently occurred since in all cases when the 2 drugs were injected simultaneously the response to prostigmine was definite, whereas

in those experiments in which 0.25 milligram of prostigmine methylsulphate alone was used the response was not definite.

7 Injection of ergotamine tartrate (0.25 mgm.) intramuscularly or 1 tablet (1 mgm.) by mouth had no discernible effect upon the colon of 4 human subjects with colostomy.

8 The simultaneous injection of ergotamine tartrate (0.25 mgm.) and prostigmine methylsulphate (0.25 mgm.) resulted in potentiation of the prostigmine. Both nonpropulsive and propulsive motilities were increased above that initiated with prostigmine (0.25 mgm.) alone.

9 Ergotamine tartrate in tablet form (1 mgm.) and prostigmine bromide in tablet form (15 mgm.) given simultaneously by mouth to the 4 human subjects resulted in the appearance of strong propulsive motility in from 1 hour to several hours after administration. The duration of action was not longer than that of 15 milligrams prostigmine bromide alone, but the greater efficiency in initiating propulsive motility which evacuated colon contents was evident.

10. The simultaneous intramuscular administration of ergotamine tartrate (0.25 mgm.) prostigmine methylsulphate (0.25 mgm.) and surgical pituitrin (1:25 units) resulted in the appearance of propulsive motility within a few minutes due to pituitrin action and the subsequent continuation of strong propulsive motility attributable to the potentiation of prostigmine by ergotamine.

11 Phystostigmine sulphate, prostigmine methylsulphate and the combinations of prostigmine with ergotamine and pituitrin facilitated the gastrocolic reflex to a meal ingested several hours after administration of the drugs.

12 It is believed that a combination of ergotamine tartrate (0.25 mgm.) prostigmine methylsulphate (0.25 mgm.) and pituitrin (1:25 units) should prove to be more effective in the management of postoperative distention than any of the drugs used alone. On the basis of duration of action, the absence of side reactions with doses which are effective in producing strong propulsive motility

prostigmine is ranked as the best single drug yet investigated.

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AMPUTATION OF THE LOWER EXTREMITIES IN OCCLUSIVE ARTERIAL DISEASES

A Ten Year Review

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THIS report is based on a study of those cases observed at the Mayo Clinic in 10 years, in which occlusive arterial disease of the lower extremities was treated by amputation. In order to make a comprehensive study we reviewed the records in groups of cases in which, respectively, the clinical diagnosis was thromboangitis obliterans, arteriosclerosis obliterans associated with diabetes, arteriosclerosis obliterans alone, and acute arterial occlusion. There were features common to all these groups, however, which should be considered (Table I).

The diagnosis of occlusive arterial disease of the lower extremities is based on the finding of diminished to absent pulsation in the femoral, popliteal, posterior tibial, and dorsalis pedis arteries. Confirmatory evidence, as would be expected, is noted more easily in the distal end of an extremity and may vary from lowered surface temperature of the part to ulcers, gangrene of the digits or frank gangrene of the foot in the more advanced cases. The most characteristic symptom is claudication, which is an aching or cramplike sensation occurring chiefly in the calf of the leg. Claudication is brought on by exercise and is relieved by rest. Other symptoms described by the patient may be coldness of the feet, a tingling sensation in the toes or changes in color such as pallor and rubor.

The diagnosis in advanced cases of occlusive arterial disease is not difficult. In early cases or in those of mild involvement, the arteries should be carefully examined as to quality of pulsation, and the skin should be observed for abnormal pallor when the affected extremity is elevated for a few minutes,

for slow return of color when the extremity is placed in dependent position after elevation, and for abnormal rubor when it has been in the dependent position for a few minutes. All these manifestations are pathognomonic of an occlusive process of the arteries.

In selecting the site for amputation, the surgeon should not be too strictly governed by standard levels, but should be guided by the blood supply as noted by means of exploratory incisions at the time of surgical intervention. Naturally, it is safer in any case of occlusive arterial disease to perform amputation above, or at the level of, the knee joint. However, in the case of a young person who has an arterial disease such as thromboangitis obliterans, an attempt to secure a satisfactory stump below the knee should be made when there is a reasonable chance to secure satisfactory healing. More will be said on this subject when thromboangitis obliterans is considered.

One type of amputation of lower extremities has been employed at the clinic fairly consistently throughout. In the thigh, a long anterior and a short posterior flap are used, with corresponding incisions throughout the muscles and fascia. The vessels are ligated doubly and the nerves are identified and injected. In some instances alcohol is used for injection, whereas in other instances 10 cubic centimeters of a 1 per cent solution of procaine hydrochloride is injected into the nerve both before and after it is severed. To our knowledge, neuromas have not formed in those cases in which procaine hydrochloride has been injected, but as to the question of the superior efficacy of either substance there is no definite proof.

In amputation below the knee a long posterior and a short anterior flap are used. The crest of the tibia is beveled and the fibula is

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TABLE I.—AMPUTATION OF LOWER EXTREMITIES FOR OCCLUSIVE ARTERIAL DISEASE
—GENERAL STATISTICS

Item	Quantity
Patients, number	140
Average age, years	56
Primary amputations, number	96.4
On males	18
On females	36
Through thigh	65
Below knee	97
Through knee (Gritti-Stokes)	
Reamputations, number	13
Postoperative gas gangrene infections, number	
Deaths	5
Deaths in entire series, number	24
Mortality rate, per cent	
Based on number of patients	
Based on primary amputations	6
Based on total amputations	8

sectioned at a level 1 inch to 2 inches (2.5 to 5 cm.) higher than the tibial amputation. When amputation is made less than 5 inches (13 cm.) below the knee the prosthesis is worn with more comfort if the fibula is fixed to the tibia or if the remaining fibular fragment is excised. Drains are employed in those cases in which there is associated lymphangitis or spreading cellulitis. The wounds are closed snugly.

We noted that in all groups of occlusive arterial disease if there is present an open lesion with gangrenous tissue, one complication is potential that is, gas gangrene infection. Such a complication followed 4.1 per cent of the primary amputations which were performed (Table I). Among the 11 patients represented by these 11 amputations, there were 5 deaths, 3 of which occurred in the group of cases of arteriosclerosis obliterans without associated diabetes. Amputation in 2 of these 3 cases was carried out, respectively at the lower and at the middle third of the thigh and in the third case, below the knee. In 2 of the 3 cases death was attributed directly to gas gangrene infection. Death in the third case occurred as the result of pneumonia on the 18th day after operation, at which time the gas gangrene infection had been controlled however one must consider the infection as contributing to the death. Death in the 2 other of the 5 cases occurred in the diabetic group and was attributed directly to gas gangrene infection. One of these 2 patients had undergone am-

putation through the thigh and the other below the knee.

From the clinical observation of the formation of gas in the soft tissues and from the recovery of *Clostridium welchii* from culture in several cases of vascular disease in which gangrene and infection developed about the toes and feet, we believe that in every case in which an open lesion is associated with gas gangrene and infection postoperative gas gangrene infection is likely to occur. Prior to surgical operation, the patients appear to possess a defense mechanism against the local presence of the organism, as is evidenced by the absence of generalized symptoms of such a malignant infection. It is likely that the superficial position of the bacteria plays a role in their failure to produce general symptoms. In those cases in which virulent gas gangrene infection develops after surgical intervention, the symptoms of undue pain, elevated temperature and rise in pulse rate are manifest, usually within 24 to 36 hours, and inspection of the stump is warranted. A less virulent infection may develop several days after amputation. The organism may be introduced into the wound at the time of amputation or may be present in the lymphatic spaces before operation. Needless to say the stump, with its traumatized muscle and fascia and some inevitable postoperative bleeding, is a fertile field for the organism regardless of its point of entrance. With definite evidence of the presence of *Clostridium welchii* in the foot before surgical operation, one is inclined to believe, if postoperative infection develops, that the organism may have been in the tissue locally and that its action may have been hurried by the surgical procedure, which provided the anaerobic condition necessary for the bacterial growth. In our experience stumps have not been protected from gas gangrene infection by prophylactic polyvalent perfringens antitoxin.

THROMBOANGITIS OBLITERANS

Thromboangitis obliterans, more commonly referred to as Buerger's disease, is a condition resulting from chronic inflammation of the blood vessels with formation of thrombus and a resultant decrease in arterial circulation to the affected part.

TABLE II—THROMBOANGITIS OBLITERANS—SITE OF PRIMARY AMPUTATION AND PRESENCE OR ABSENCE OF POSTOPERATIVE COMPLICATION

Complication	Patients or procedure	Site of primary amputation						Totals
		Below knee		Through thigh		Through knee (Gritti-Stokes)		
		Patients*	Primary amputations	Patients*	Primary amputations	Patients*	Primary amputations	
Present	Patients*	25		3		1		29
	Primary amputations		25		3		1	29
Absent	Patients*	33		26		1		60
	Primary amputations		38		29		1	68
Total		58	63	29	32	2	2	

*The number of patients represented in this table adds to 89. Actually there were only 83 patients. The discrepancy arose because 6 patients underwent primary amputation of one lower extremity without complication resulting but also underwent primary amputation of the other lower extremity with complication resulting. These 6 patients are counted both in the group in which complications were present and in that in which they were absent.

Thromboangitis obliterans affects, primarily, middle aged persons. It occurs chiefly among men, although it is not confined to males as has been previously thought. However, there were no women in the group of patients who, in the ten years from 1930 to 1939 inclusive, required amputation of one or both lower extremities for thromboangitis obliterans at the clinic. If either lower extremity must be removed for this disease, the patient should plan for a stay in the hospital of about 3 weeks. For our group of 60 patients whose recovery was uncomplicated (Table II) the average period of hospitalization, after the primary surgical intervention, was 21 days. Various methods of anesthesia may be used.

Little need be said, in addition to what is shown in Table II, concerning the site of primary amputation and the incidence of postoperative complications. The nature of the complications and the necessary secondary measures, however, have a bearing on the results and merit some remark.

Of the 25 primary amputations below the knee, which resulted in complications (Table II), 22 were followed by reamputation and 3 were not. Of the 22 reamputations, 7 were below the knee and 15 above. Following 2 of the 7 amputations and 3 of the 15 amputations just mentioned, gas gangrene infection occurred. In 1 of these 5 cases of gas gangrene, the blood stream became infected. Concerning the 25 amputations mentioned in the first

sentence of this paragraph it has been indicated that following 3 of them reamputation was unnecessary. Of these 3 amputations, subsequent to 2 of them, infection took place and subsequent to the third, a slowly healing ulcer developed.

Referring to Table II again. Of the 3 primary amputations through the thigh, which resulted in complications, 1 was followed by reamputation and 2 were not. Of the 2 instances just mentioned, the complication consisted in infection in one and a slowly healing ulcer in the other. The one amputation through the knee (Gritti-Stokes), which is found in the same category in Table II as the cases just considered, was followed by reamputation.

From what has just been said of reamputation, as well as from what is evident in Table II concerning the site of primary amputation, those who previously have been interested in the subject will deduce that in this group of middle aged men, more careful effort is made to amputate at the lowest level of circulatory adequacy than in any other group of patients. Although application of this principle results in a relatively high percentage of reamputations, there were no deaths in the group just reported, only one general complication occurred, and a serviceable stump below the knee was obtained in 76 per cent of the cases. We believe that this result justifies trial of primary amputation below the knee in a large percentage of those cases of thromboangitis

TABLE III—ARTERIOSCLEROSIS OBLITERANS WITHOUT DIABETES—SITE OF PRIMARY AMPUTATION, PRESENCE OR ABSENCE OF POSTOPERATIVE COMPLICATIONS AND THE MORTALITY

Complications	Patients or procedures	Site of primary amputation					
		Below knee		Through thigh		Totals	Deaths
		Patients*	Primary amputations	Patients*	Primary amputations		
Present	Patients*	6		16		22	3
	Primary amputations				16	22	
Absent	Patients*	8		12		20	
	Primary amputations				12	20	
Totals		14	0	28	28		

*The number of patients represented in this table adds to 84. Actually, there were only 80 patients. The discrepancy arose because patients underwent primary amputation of one lower extremity without complication resulting but also underwent primary amputation of the other lower extremity with complication resulting. These patients are counted both in the group in which complications were present and in that in which they were absent.

obliterans in which amputation must be performed.

ARTERIOSCLEROSIS OBLITERANS WITHOUT DIABETES

In our series of surgical amputations for vascular deficiencies the cases in which diagnosis was made of arteriosclerosis obliterans without diabetes rivaled in number the cases of thromboangiitis obliterans. Clinically however these 2 conditions presented wide variance in statistical findings.

Seventy of the patients were males and 10, females. Because of the advanced age of these patients one would anticipate the presence of complicating conditions. Acceptable methods of anesthesia, therefore are fewer than the methods acceptable in cases of thromboangiitis obliterans. We favor spinal anesthesia in the presence of arteriosclerosis obliterans.

As is indicated in Table III of the 32 patients who experienced postoperative complications, 13 died. Of these 13 patients, 12 had been subjected to primary amputation through the thigh and of one the primary amputation was below the knee. The death of 3 of the 13 patients was attributed to bronchial pneumonia of 2 to coronary disease with congestive heart failure of 2 others to cerebrovascular accidents of 2 to uremia of 1 to multiple emboli and of 3 to gas gangrene infection. These are in contradistinction to 5 cases of thromboangiitis obliterans in which gas gangrene infection occurred after surgical intervention, with no resultant deaths

In the 9 remaining instances of the 22 in which postoperative complications occurred, the difficulty arose in healing of the stump. In 3 instances in which postoperative complications occurred and reamputation was not required, convalescence after primary amputation through the thigh was complicated by slow healing because of circulatory deficiency. Six patients, or approximately 8 per cent of the 80 patients in this group were subjected to reamputation before a satisfactory stump was obtained. It is interesting to note that 4 of the 6 reamputations were done on patients who had been subjected to primary amputation below the knee. The outstanding fact brought out in this series of 80 cases then is that, because of the 2 interdependent factors of advanced age and consequent complicating conditions 82 per cent of the primary amputations were through the thigh (Table III). Amputation below the knee should be reserved for the younger patients.

ARTERIOSCLEROSIS OBLITERANS WITH ASSOCIATED DIABETES

Arteriosclerosis obliterans with associated diabetes furnished the third largest number of cases in our series of amputations for occlusive arterial disease. In this group patients were in their late years of life. The proportion of men was not so marked as it was in the preceding groups of thromboangiitis obliterans and arteriosclerosis obliterans without diabetes. However, it again demonstrates among pa-

TABLE IV—ARTERIOSCLEROSIS OBLITERANS WITH ASSOCIATED DIABETES—SITE OF PRIMARY AMPUTATION AND PRESENCE OR ABSENCE OF POSTOPERATIVE COMPLICATION

Complication	Patients or procedures	Site of primary amputation					
		Below knee		Through thigh		Totals	Deaths
		Patients*	Primary amputations	Patients*	Primary amputations		
Present	Patients*	9		9		18	7
	Primary amputations		9		9	18	
Absent	Patients*	10		35		45	0
	Primary amputations		10		38	48	
Totals		19	19	44	47		

*The number of patients represented in this table adds to 63. Actually there were only 61 patients. The discrepancy arose because 2 patients underwent primary amputation of one lower extremity without complication resulting but also underwent primary amputation of the other lower extremity with complication resulting. These 2 patients are counted both in the group in which complications were present and in that in which they were absent.

tients who are suffering with arterial disease, as 42 of the patients were men and 19 were women.

We favor employment of spinal anesthesia. The size of the dose should be governed by the general condition and size of the patient. It is better to err in the giving of an insufficient amount of anesthetic agent for completion of the operation and to rely on supplemental agents, such as pentothal sodium, than to give large doses of the spinal anesthetic substance.

As is indicated in Table IV, 72.7 per cent of the primary amputations were followed by an uncomplicated postoperative course. Of the 18 patients who experienced postoperative complications, 7 died. Five of these 7 patients had been subjected to primary amputation through the thigh and of 2 of the 7, the primary amputation was below the knee. The deaths of 2 of the 7 patients were attributed to bronchial pneumonia, of 2, to unknown cause, of 1, to renal failure, and of 2, to gas gangrene infection. Both of the patients who died from gas gangrene infection underwent previous amputation below the knee.

In the 11 remaining cases of the 18 in which postoperative complications occurred, the difficulty arose in healing of the stump. In 6 of the 11 cases, convalescence was complicated by slow healing as a result of inadequate circulation. The postoperative course of 3 patients was complicated by infection and sloughing. In the 2 remaining cases of the 11 the complications were inadequate circulation and gas gangrene infection, respectively, both

of these patients were subjected to primary amputation below the knee, and both were subjected to reamputation. Nine, or 47.4 per cent, of the 19 primary amputations below the knee were followed by complications.

The obvious fact brought out in our series of patients with arteriosclerosis obliterans is that the association of diabetes did not increase the mortality rate but that this was found to be less than the mortality rate in those cases of arteriosclerosis obliterans without associated diabetes. This fact may be attributed to the close co-operation of the internist and the surgeon, both in the preoperative preparation and the postoperative care of the diabetic patient. It is further shown that amputations below the knee should be reserved for the exceptional case in the younger patients.

ACUTE ARTERIAL OCCLUSION

The final group of cases, those of acute arterial occlusion, was the smallest group in the series. It is composed of 16 patients (10 males and 6 females) on whom 16 primary amputations were performed, 15 through the thigh and 1 a disarticulation at the hip. There was no case in which bilateral amputation was necessary. Although the patients in this group were young, with an average age of 52 years (Table V, A), they constituted the greatest operative risk and carried the highest mortality rate of any group studied. Ten of the patients presented clinical evidence of severe heart disease before operation, 3 of the 10 having rheumatic cardiac lesions. Among

TABLE V A — ACUTE ARTERIAL OCCLUSION
AGE DISTRIBUTION

Age, years	Patients	Per cent
30-39	6	37.5
40-49	3	18.7
50-59	4	25
60-69	6	37.5
70 or more		0
Total	16	100
Youngest, years	7	
Oldest, years	73	
Average, years		

TABLE V B — ACUTE ARTERIAL OCCLUSION
ANESTHESIA

Type of anesthesia	Patients operated on	Kendall's complication present	% complications	Deaths
General				
Intubation				
Perineural anesthesia (with or without)				
Total	16	1	6.25	3

the 16 patients there were 4 deaths a mortality of 25 per cent for the group (Table V B). One patient died of bronchial pneumonia on the 21st day after operation the second died on the 1st day after the surgical procedure and a third on the 2nd day both deaths resulting from cardiac complications. A fourth patient died of cerebral embolism on the 9th day after operation in this case the wound was healed and the patient had been dismissed she died at her home. Two of the deaths were of women and 2 of men. In 12 or 75 per cent of the cases the left lower extremity was involved.

In this group of 16 cases, the femoral artery was occluded in 5 the popliteal artery in 10 and the posterior tibial artery in 1 case. In only 2 of the cases was there any degree of circulatory involvement of the opposite extremity. In cases in which lesions were of the left side the popliteal artery was occluded in 9, the femoral artery in 2 and the posterior tibial artery in 1 case. Of these patients 6 were men and 6 were women. In cases in which lesions were of the right side the femoral artery was occluded in 3 and the popliteal artery in 1 case none of the patients were women and no deaths were reported. The average duration of occlusion before surgical intervention with the exception of 1 case

in which a gangrene infection was of 1 year a duration was found to be 12.6 days and the average period necessary for healing after amputation was 27.7 days. In 9, or 56 per cent of the cases, the postoperative course was uneventful and primary healing occurred. In 2 cases healing was delayed 38 and 32 days, respectively. In a third case reamputation was required but healing took place on the 13th day thereafter.

COMMENT AND SUMMARY

We believe that the discrepancy in the mortality rate among the many reports is caused by the difference in environmental factors and in facilities for treatment rather than by differences in surgical technique and the varying capacity of the surgeon. There should be the closest harmony between the internist and the surgeon for the utmost efficiency in handling cases of occlusive arterial disease. Occlusive arterial disease is a condition most frequently seen in men although it is not uncommon in women. The ratio found in the series we are presenting was approximately 6.5:1. However a more nearly equal ratio was seen in arteriosclerosis with diabetes and in acute arterial occlusion. Thromboangiitis obliterans rarely affects women.

If the individual with occlusive arterial disease is of a younger age group and more especially if he has thromboangiitis obliterans, one should seek the level of circulatory adequacy for amputation. For the more elderly patients, usually found in one of the arteriosclerotic groups, amputations below the knee should be discouraged.

A complication common to all groups of occlusive arterial disease is gas gangrene infection following amputation especially in cases in which amputations are done below the knee. As we said early in this paper the value of prophylactic polyvalent perfringens antitoxin is questionable. The value of therapeutic polyvalent perfringens antitoxin has been proved. Sulfonamide drugs in postoperative infections have been proved valuable adjuncts to the armamentarium of the surgeon in cases of spreading cellulitis or associated lymphangitis in occlusive arterial disease one of the sulfonamide preparations may be ad-

vantageously placed in the wound at the time of amputation. In general, wounds should be closed snugly unless there is some definite indication for drainage at the time of the amputation.

Hasty amputation with only emergency preparation before operation is indicated only in cases of gangrene with spreading cellulitis, gas gangrene infection, or gangrene associated with diabetes in which the diabetes is uncontrollable.

Review of the cases of acute arterial occlusion suggests that this condition has a predi-

lection for the left side and in all the cases of our series, amputation below the knee was precluded. In our opinion, acute arterial occlusion is not an emergency condition requiring immediate amputation, in the majority of cases the surgeon may safely wait for establishment of collateral circulation and a line of demarcation. Further, in acute arterial occlusion, one may anticipate a high mortality rate. This is explained by the fact that the condition which necessitates amputation is, as a rule, a complication of some underlying severe systemic pathological change.

EXTERNAL BILIARY FISTULAS

A Study of 23 Cases

N. FREDERICK HICKEN, M.D., LESLIE B. WHITE, M.D., and Q. B. CORAY, M.D.
Salt Lake City, Utah

PERSISTENT external fistulas occasionally follow surgical attacks on the extrahepatic biliary system. These tantalizing complications annoy the patients and harass the surgeons for both realize that the primary operations have failed to remove the obstructive lesions which were interfering with the free flow of bile and associated secretions into the duodenum. Corrective therapy requires the removal of the obstructions or the formation of new biliary channels.

This study is based on an analysis of 23 cases of postoperative biliary fistulas which have followed routine operations for gall stones. Etiologically they may be divided into three groups: those due to incomplete removal of the primary obstructions, those caused by surgical accidents, and those in which the external sinuses were planned for decompressive purposes only.

Incomplete primary operations accounted for 88 per cent of the persisting fistulas. This means that the provocative obstructions were not removed either because the operators did not recognize them or were incapable of performing the necessary corrective procedures. Ninety-five per cent of the initial explorations were for gall stones but in 20 instances these elusive calculi were incompletely removed. In 12 cases, 60 per cent, stones were left in the common bile duct; in 6 instances, 30 per cent, they were not removed from the gall bladder; in 1 patient multiple stones were left in the cystic duct, and in another they were overlooked in both the gall bladder and cystic duct. In every instance the operative notes stated that all stones had been removed and it was not until the draining sinuses refused to heal that true appraisals were made.

It was interesting to note that 57 per cent of the external fistulas followed cholecystotomies while only 43 per cent occurred after cholecystectomies. The higher incidence occurring with simple drainage of the gall bladder can be explained by the fact that the majority of the primary operations were performed in small rural hospitals or in charity institutions where the younger men were acquiring experience. It may be argued that the group submitting to cholecystostomy were too ill to undergo a more formidable operation but such was not the case. Studies of their hospital records reveal that all these cases were scheduled for cholecystectomies, but conditions were encountered which compelled the "occasional operator" to employ simple drainage. Ballfour and Ross estimate that 90 per cent of their 166 cases having biliary fistulas resulted from a failure to remove the gall bladder at the initial operation. They affirm that in performing a cholecystectomy the cystic and common bile ducts must be exposed thus minimizing the possibility of overlooking a migratory stone. No one who can not recognize and cope with choledochal lesions should attempt to operate for gall stones.

Surgical accidents such as, ligation, severance and crushing of the common bile duct account for a small percentage of these fistulas. On 2 occasions the choledochus was accidentally clamped while the surgeon was attempting to control annoying hemorrhages. Inexperience, inadequate exposure and speedy haphazard work propagate such errors.

Therapeutic external fistulas may be deliberately formed so as to decompress an obstructed biliary tree. For example a cholelith may be so intense or the patient's condition so precarious that palliative drainage is imperative. Remedial operations are not employed until definite improvement has been made.

From the Surgical and Roentgenological Services of the Dr. Lewis Memorial Latter Day Saints Hospital.

Short-circuiting procedures, such as cholecystoenterostomies, choledochenterostomies, and hepaticoenterostomies are preferred to external drainage but unfortunately they cannot always be employed. In one instance we encountered such a generalized fibrosis of the choledochus and common hepatic duct that the formation of an external fistula afforded the only surcease from the intractable pruritis.

PREVENTION

An appreciation that 95 per cent of these external sinuses occur as unexpected complications following operations for gall stones emphasizes the importance of prevention. The observance of certain accepted surgical principles will greatly minimize the incidence of these tantalizing errors.

A The importance of an accurate clinical diagnosis cannot be overestimated. It is not sufficient to know that the patient has gall stones but one should determine whether there may be a complicating cholangitis, acute cholecystitis, cholemia, or hepatic insufficiency. To be unexpectedly confronted by these serious complications may necessitate a simple cholecystostomy without being able to determine the functional status of the bile ducts. In 5 such instances the failure to recognize the presence of acute cholecystitis before operation necessitated conservative operations with the result that choledochal stones were not discovered and chronic fistulas resulted.

B Adequate preoperative preparation and proper timing of all surgical interventions are absolutely essential in preventing such complications. The improperly prepared jaundiced patient is no candidate for exploration of the bile ducts. Likewise, the failure to provide ample time for acute infections to subside may necessitate palliative measures. For example, an acute cholecystitis usually responds to conservative therapy and extensive remedial operations can be safely employed during the quiescent phase which would be forbidden during the height of the inflammatory reaction. It is here that experience and judgment pay the highest returns.

C It is obligatory that the functional status of the bile duct should be accurately determined before any type of extirpative



Fig 1 The gall bladder, cystic duct, choledochus and duodenum were all visualized by the introduction of 55 cubic centimeters of diodrast, 70 per cent, into the external sinus. Note the gall stones partially occluding the orifice of the cystic duct, thus interfering with the emptying of the gall bladder and accounting for the biliary fistula.

surgery is undertaken. It has been our practice to explore the common bile duct if it contains stones, if it is dilated or indurated, if there has been an antecedent jaundice, if there is an inflammatory pancreatitis, and if unable to find other causes for the bilogenic dysfunctions.

While these indications for choledochotomy are definite, unfortunately the recognition of their presence is a matter of individual interpretation. What is thought to be normal by one surgeon may be considered pathological by another. It is the border line case which gives us the most concern and provides the most fertile field for errors. Visual inspection and palpatory examinations often fail to detect the incomplete choledochal obstructions. Errors of omission can be entirely prevented by the employing of cholangiographic studies during the operation (5). If the bile ducts appear patent and the contrast fluid flows unhampered into the duodenum no further exploration is warranted. If, however, obstructive lesions are visualized, the proper remedial procedure can be employed. The diagnostic cholangiograms are accurate and give the surgeon a sense of security.

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Fig. 1. a, Postoperative cholangiogram reveals dilated biliary tree. b, Complete obstruction of the ampulla of Vater for the contrast media does not pass into the duodenum. b, Some 8 weeks later. The external decompression has permitted the pancreas to subside partially for the duodenal flow around the stone and escapes into the duodenum. Note the thread-like pattern of the ampulla of Vater which is indicative of pancreatitis. This patient was not jaundiced after operation and the stone healed spontaneously in spite of the choledochal stone.

D. External fistulas can be prevented if the postoperative studies detect provocative obstructions, thereby permitting immediate corrective therapy. Every patient submitting to a cholecystostomy or a choledochotomy should have a complete cholangiographic study before the drainage tubes are withdrawn (6). When the ducts appear patulous the drains can be removed with impunity. Should pathological obstructions be present they can be diagnosed by the recognition of their identifying characteristics. For example gall stones cast "incriminating negative shadows" while blood clots and inspissated plugs of mucus produce pleomorphic filling defects which float around within the ducts (Fig. 1). Pancreatitis exerts a concentric compression of the ampulla of Vater so that when the contrast fluid passes through the narrowed ductal lumen it forms a distinctive thread-like pattern (Fig. 2). Carcinoma of the pancreas produces a slow but progressive obstruction of

the ampulla of Vater resulting in a tremendous dilatation of all other segments of the biliary tract. Biliary dysynergia is characterized by a temporary but complete obstruction of the terminal choledochus which spontaneously disappears as the spastic contractions of the sphincter of Oddi subside.

When the postoperative cholangiograms demonstrate a choledochal stone attempts should be made to dislodge it by means of the biliary flush. Best and Hicken (2) have succeeded in washing residual calculi from the ducts into the intestinal tract, thereby obviating a second exploration. They suggest that the sphincter of Oddi be completely relaxed by the administration of nitroglycerine and atropine sulfate before the drainage tube and choledochus is lavaged with warm olive oil. By these ductal irrigations they "flushed stones" from the common bile duct into the duodenum and recovered them in the feces (3). Butsch, McGowan, and Walters follow



Fig 3 This fistula closed 1 week after removal of the T tube in spite of choledochal stones. It is apparent that the calculi are not completely obstructing the duct. The rapidity with which the fistula healed, the absence of jaundice, and quick recovery of the patient gave no clinical signs of the overlooked stones, this emphasizes the value of cholangiograms.



Fig 4 A woman, 76 years old, suffered from a perforation of an acute gangrenous gall bladder. A cholecystostomy with extraction of 2 large gall stones was performed. Deferred cholangiograms revealed an incarcerated ampullar stone which was overlooked at the primary operation. The resulting fistula healed spontaneously within 8 weeks in spite of the choledochal stone.

ing the suggestion of Pribram, dissolved the migratory stones by the intraductal instillations of ether. While both of these methods should be utilized before subsequent operations are resorted to, unfortunately they seldom accomplish the desired objectives. We have, however, been able to dissolve plugs of mucus and blood clots by irrigating the common bile duct with a solution of the essence of caroid.

If conservative procedures fail to remove the offending obstruction, operative intervention should be employed as soon as the patient's condition permits. It is unwise to wait for a permanent sinus to form, for fear that an ensuing cholangitis, hepatitis, cholemia, or hepatic insufficiency might complicate the problem.

CLINICAL FEATURES

It has been our experience that when the cholangiograms revealed the ducts to be patulous that all external drainage subsided within 3 days after the drainage tubes were with-



Fig 5 Postoperative cholangiograms visualize choledochal stones that had been overlooked at the time of the primary operation. The patient was not jaundiced, the external sinus drained for 10 weeks, then it closed spontaneously in spite of the fact that ampullar stones were present.



Fig. 2. a, Postoperative cholangiogram reveals dilated biliary tree with complete obstruction of the ampulla of Vater for the contrast media does not pass into the duodenum. b, Some 8 weeks later. The external decompression has permitted the pancreatitis to subside partially for the diaphragm flow around the stone and escapes into the duodenum. Note the thread-like pattern of the ampulla of Vater which is indicative of pancreatitis. This patient was not jaundiced after operation, and the stone healed spontaneously in spite of the choledochal stone.

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saline, it may become clogged. Likewise, if the secretions are mucoid or hemorrhagic they tend to obstruct the tube and inhibit free drainage. This can be prevented by filling the T tube with a solution of the essence of caroid which liquefies the clots and dissolves the mucus. As soon as bile is detected in the stools, the drainage tube can be clamped so as to force this essential secretion into the duodenum. If the flow of bile is sluggish the administration of dehydrocholic acid acts as a cholagogue thus producing an effective physiological biliary flush. Should there be a spastic contraction of the sphincter of Oddi, this may be supplemented by the use of nitroglycerine and atropine sulfate.

How long shall the common bile duct be drained? Cholangiography affords the only accurate answer to this question. When the cholangiograms demonstrate the bile ducts to be patent then the drainage tubes can be safely removed. Should there be a residual pancreatitis or cholangitis, the external drainage must be continued until these inflammatory reactions have subsided (Fig 7).

RESULTS

Twenty-three patients with external biliary fistulas underwent 28 separate operations with a mortality rate of 26 per cent. It was interesting to note that in 16 private cases there was but 1 death, 6 per cent. This does not mean that the charity patient does not receive the same conscientious treatment as the private client but rather that the former neglect to seek early therapy because of economic embarrassment.

An analysis of the causes of death emphasizes the dangers of late complications. One patient, having had a fistula for 11½ years and persisting jaundice for 6 months, died because of hepatic shock incidental to an extensive cirrhosis. Carcinoma of the liver proved fatal to 1 woman who had suffered

with a draining sinus for 36 months. Post-operative hemorrhage accounted for 1 death but this was before vitamin K therapy was fully understood. Pylephlebitis, biliary peritonitis, hepatic, subhepatic, and subphrenic abscesses likewise exacted their toll. It is evident that the majority of these complications could have been prevented by timely surgery.

SUMMARY

- 1 Twenty-three cases of persistent external biliary fistulas are presented with particular reference to etiology, prevention, diagnosis, and treatment.
- 2 Ninety-five per cent of these fistulas occurred as complications following cholecystostomy and cholecystectomy.
- 3 The failure to remove all the gall stones at the primary operation accounted for 88 per cent of the fistulas.
- 4 The indications for and the technique of preoperative, operative, and postoperative cholangiography are presented.
- 5 The diagnostic and therapeutic value of cholangiograms is emphasized by case presentations.
- 6 The surgical and postoperative management of the various types of biliary fistulas is given.

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TESTICULAR BIOPSY FURTHER STUDIES IN MALE INFERTILITY

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In 1940 one (2) of us reported studies on testicular biopsy and its application in the diagnosis of male infertility. This procedure consists of the removal of a minute piece of tissue from the periphery of the testis through a small incision in the scrotum. It is a simple innocuous procedure and may be performed in the office under local anesthesia. In our experience there have been no undesirable after-effects, every patient resuming his usual activity the next day.

While the performance of biopsy was at first limited to instances of azoospermia, it soon occurred to us that this procedure could be utilized in patients with any type of spermatogenic deficiency whether it be morphological or numerical. The more biopsies performed the better we appreciated the superiority of this method over any other procedures. The two older methods available today are aspiration of the testis and the manifold biological studies of the ejaculate. Testicular aspiration even when spermatozoa are obtained gives merely quantitative data and is valuable only in the differential diagnosis between obstructive and nonobstructive azoospermia. In the study of the ejaculate the finding of a large percentage of abnormally formed spermatozoa points only to faulty spermatogenesis. Both these older methods, however fail to give information regarding the nature of the intrinsic lesion in the seminiferous tubules. The insight into actual pathogenesis, as revealed by testicular biopsy, is in our opinion, the *sine qua non* in a thorough study of male infertility.

The present series of testicular biopsies, performed as part of the study on males with reduced fertility numbers 95. This series comprises a variety of pathological types including instances of both testicular under-

development resulting from a congenital endocrine imbalance and testicular degeneration of a normally developed testis brought about by inflammation toxic processes, or post pubertal endocrine disturbances. An analysis of the findings indicates that these two lesions can be differentiated by the data obtained through testicular biopsy and that this differentiation as will be shown is of utmost importance in determining the prognosis and type of treatment. Lest the objection be raised that the tissue obtained through biopsy may not necessarily be representative of the entire gland it should be pointed out that large sections of normal testis obtained at autopsy done immediately after death show a general uniformity of the seminiferous tubules (Fig. 1) and also that sections of biopsies from different portions of the same testis obtained at intervals of 6 weeks show similar pathological processes throughout.

THE NORMAL SEMINIFEROUS TUBULE

A cross section of a testis shows two distinctly different types of tissue the seminiferous tubules, in which spermatogenesis takes place and the interstitial tissue which contains the cells of Leydig. In the seminiferous tubules the successive phases of spermatogenesis are arranged according to a definite sequence. The youngest and least developed cells are situated on the basement membrane of the tubule, the *membrana propria*, while the mature forms are more centrally located. Accordingly the spermatogonia, the cells in which spermatogenesis begins, and the next generation, the primary spermatocytes, remain in their early growth phases adjacent to the basement membrane. Advancing toward the center the primary and secondary spermatocytes are seen undergoing division and further development. The next layer of cells is composed of groups of sperma-

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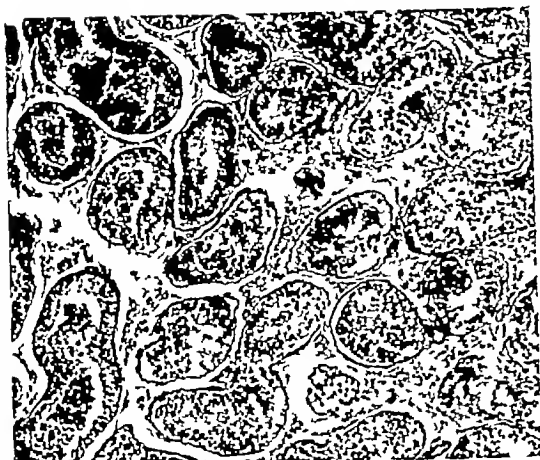


Fig 1 Typical portion of testis, removed at autopsy immediately after death, illustrating uniformity of tubules ($\times 60$) (Formalin fixed)



Fig 2 Normal seminiferous tubules Note presence and regular arrangement of various generations of spermatogenic cells Membrana propria of normal thickness ($\times 150$)

tids Finally and innermost, one sees groups of immature spermatozoa (Fig 2)

In addition to these spermatogenic elements, the seminiferous tubule shows another type of cell, the so called cells of Sertoli These are slender, columnar elements standing upright on the basement membrane and spaced at fairly regular intervals They are presumably supporting elements, though some consider them capable of developing, under certain conditions, into true spermatogenic cells

The wall of the seminiferous tubules, the membrana propria, consists of thin collagenous fibers and a delicate elastic network, and varies in thickness from 3 to 6 microns The interstitial tissue—the tissue between the tubules—consists of thin collagenous fibers, blood and lymph vessels, nerves, and several varieties of cells—fibroblasts, resting wandering cells, mast cells, embryonic perivascular cells, and the interstitial cells of Leydig which are believed to elaborate the internal secretion of the testis

Occasionally one notes seminiferous tubules showing degenerating spermatogenic cells involving all generations, particularly spermatocytes and spermatids Such degenerating cells lose their connection with the rest of the epithelium, are cast off into the lumen, and disintegrate into granular and fatty debris Tubules exhibiting such degenerative changes,

if not excessive, need not be considered pathological, especially if they are surrounded by tubules with normal spermatogenesis in full progress

THE PATHOLOGICAL SEMINIFEROUS TUBULE

Careful study of the 95 testicular biopsies herein reported revealed that the pathological changes, although varying considerably in degree, could be separated into two distinct types (1) intratubular—those in which the degenerative or developmental lesion is confined solely to the seminiferous tubules, and (2) peritubular—those in which peritubular fibrosis, either inflammatory or replacement, is seen in addition to the intratubular lesion

Of the 95 biopsies 16 showed normal spermatogenesis Of the 79 remaining, 51, or 65 per cent, showed moderate to marked peritubular fibrosis, while only 28, or 35 per cent, showed a normal amount of peritubular connective tissue despite definite damage to the tubular epithelium

Type I Intratubular lesions The pathological changes confined to the tubules have been found to vary in severity from simple desquamation of the innermost layer of cells, the spermatids, to more severe degenerative changes in which both the spermatocytes and spermatogonia are involved or, finally, to a stage in which the tubule consists of merely a single layer of undifferentiated cells appar-



Fig. 3. Case . . . Section of testis, before treatment, showing mostly disorganization and incomplete epithelial differentiation. Only the large tubule appears capable of producing spermatozoa. No peritubular fibrosis ($\times 50$).



Fig. 4. Case . . . Section from surgically corrected cryptorchid testis showing trophic tubules lined by single layer of undifferentiated cells. Peritubular fibrosis ($\times 50$).

ently incapable of growth and division. In the milder cases, the younger cell forms are not affected and differentiation into spermatids continues. Under such circumstances, further cell growth is interrupted and a testicular biopsy reveals an increase in the number of spermatids. In the more severe forms degeneration is more pronounced a great deal of debris often being seen in the lumen, and the tubule is lined with only one or two layers of cells.

Whatever the etiological factors may be the intratubular degenerative process may be halted at any point and, since the basal layer of cells, the spermatogonia, has not been affected regeneration may take place under suitable circumstances. Thus if the disturbing factor be a pituitary deficiency restoration to normal could be effected by the administration of a pituitary gonadotropic substance.

The 4 cases cited are selected from a group of 28 showing intratubular damage only. Of these 28 improvement in the semen picture or biopsy or both followed the administration of equine gonadotropin in 11 instances. These 11 cases, we believe are patients with mild insufficiency of pituitary gonadotropin. The

7 remaining cases probably represent either testicular lesions of nonendocrine etiology or are instances of endocrine deficiency so advanced that regeneration following treatment

with the gonadotropins at present available has not occurred.

CASE 1. Mild degree of tubule damage without fibrosis. G. C. aged 29 years, had moderate amount of girdle obesity. Basal metabolic rate was -8. Semen examination revealed a total count of 9,000,000 spermatozoa, of which 38 per cent were morphologically normal. Following the administration of an equine gonadotropin the total sperm count as raised to 20,000,000 with only 20 per cent abnormal forms and with corresponding improvement in the histological picture (Fig. 3).

CASE 2. Severe tubular damage without fibrosis. F. L. aged 28 years. This was an instance of under development in a man with cryptorchidism which had been surgically corrected at the age of 25 years. The testes measured 3.5 by 2.0 centimeters in size. Semen examination showed azoospermia. There was no response to the administration of equine gonadotropin (Fig. 4).

CASE 3. Volutular degeneration (thick fibrosis). F. S., aged 5 years, had been given 5 milligrams of testosterone daily for a total of 450 milligrams in order to suppress his hypermetabolism which had resulted in repeated incarcerations for criminal rape. His testes were reduced to two-thirds of their original size and his libido was so suppressed that a semen specimen could not be obtained. It is important to note that during this period of testicular degeneration, he had no symptoms referable to the testes (Fig. 5). Ten months following the cessation of therapy, second biopsy showed pronounced evidence of regeneration. Libido had returned to normal (Fig. 6).

Hypermetabolism of childhood, undetected degeneration, being reported (prior death) by Dr. C. W. Drake.

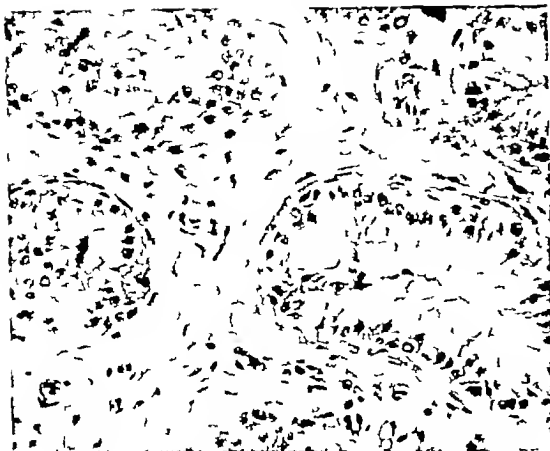


Fig 5 Case 3 Section from stilbestrol induced degeneration. Tubules are lined by only one or two layers of healthy cells and display central necrosis. Note interstitial edema and absence of peritubular fibrosis ($\times 150$)

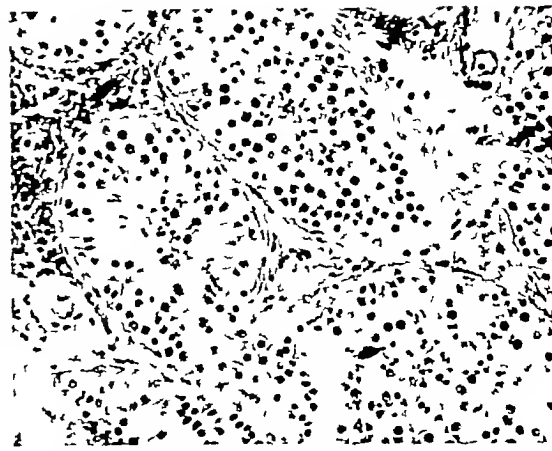


Fig 6 Case 3 Section from same patient as in Figure 5, 2 months after cessation of stilbestrol, showing restoration. Regenerative process proceeding, but not yet complete. Note focal fibrosis ($\times 150$)

CASE 4 Tubular underdevelopment and degeneration without fibrosis. S. G., aged 29 years, displayed many of the stigmas of hypogonadism. He shaved his beard once a week. He had trochanteric obesity, with a prominence of the breasts and abdominal fat. The penis was small, the testes measured 2.5 by 1.5 centimeters. Semen examination revealed azoospermia (Fig 7). He received intramuscular injections consisting of 40 milligrams of testosterone propionate and 120 international units of equine gonadotropin weekly for a period of 4 months. Re examination revealed no change in size of testes, an increase in size of penis, with normal

libido and potentia. There was no improvement in the semen (Fig 8).

Type II Peritubular fibrosis The presence of peritubular fibrosis is indicative of either the end stage of an inflammatory process or of a severe degenerative process which has produced, in addition to epithelial damage, an infolding and thickening of the membrana propria, a shrinkage of the tubules, and subsequently replacement fibrosis. Such peri-



Fig 7 Case 4 Section from patient with hypogonadism. Marked underdevelopment. Note small size of tubules. No peritubular fibrosis ($\times 150$)

(This tissue was fixed with formalin.) All other tissue, except that used in Figure 1, were fixed with a modified (B. McClung) Bouin's solution

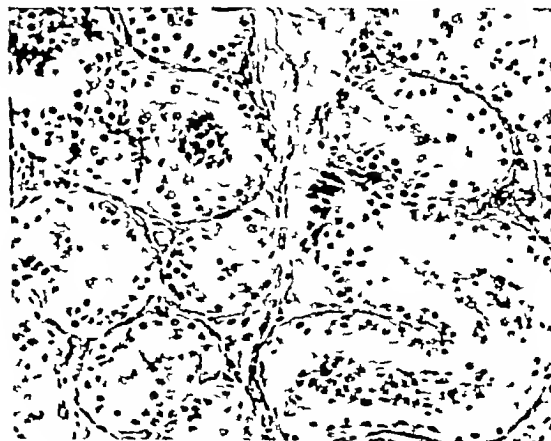


Fig 8 Case 4 Section from testis of hypogonad after treatment with testosterone propionate. No increase in size of tubules or in the number of epithelial layers. Note appearance of necrosis and its similarity to stilbestrol induced necrosis of Figure 5 ($\times 150$)

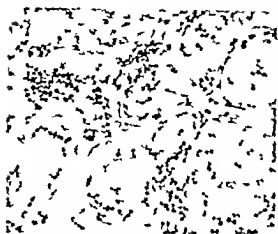


Fig. 9. Case 5. Section from testis showing degeneration following upon an inflammatory process. Note small degenerated tubules, thickening of intertubular propria, and peritubular fibrous tissue. ($\times 50$)

tubular fibrosis must not be confused with the apparent increase in the number of interstitial cells of Leydig—a phenomenon caused by a relative reduction in the size of the tubules. The importance of this peritubular fibrosis is that it signifies an accompanying involvement of the membrana propria adjacent to the mother cells, the spermatogonia, and implies previous injury to them. The degree of peritubular fibrosis varies from a simple thickening of the membrana propria to instances in which the fibrous ring is as thick as the tubule itself. In the most advanced cases, fibrosis is represented by actual scarring with complete obliteration of the tubules.

It is of the utmost importance to note that not one of the patients with peritubular fibrosis, even of the mildest degree, responded to the administration of equine gonadotropin. The 2 cases cited are selected from a group of 51 showing tubular damage associated with varying degrees of peritubular fibrosis.

CASE 5. Mild tubular damage associated with generalized peritubular fibrosis. D. L. aged 3 years, showed no evidence of endocrine disturbance. H. g. no history of pain or swelling of the testes, which were normal to palpation. Testicular sperm count was 6,000,000 with 4 per cent abnormal forms. In addition to the microscopic picture there was also gross evidence of previous inflammation of the testes. At biopsy the scrotal layers of the scrotum, particularly the parietal layer of the tunica vaginalis testis, were thickened, and there was an excess of

hydrocele fluid present. The administration of equine gonadotropin failed to produce any change in the semen picture (Fig. 9).

CASE 6. Severe tubular damage accompanied by generalized peritubular fibrosis and partial obliteration. A. L. aged 3 years, exhibited marked familial, evenly distributed obesity. H. g. no history of testicular disease. Basal metabolic rate was -4 . Roentgenogram of sella turcica normal. The right testis as normal, the left definitely reduced in size. During the performance of testicular biopsy gross evidence of previous inflammation was apparent. On the left side the two layers of the tunica vaginalis testis were adherent. Semen examination revealed total of 9,000,000 spermatozoa, 15 per cent abnormal forms, which undoubtedly originated in the right testis. Treatment with equine gonadotropin failed to produce any change in the semen (Fig. 1).

CORRELATION OF TESTICULAR BIOPSY AND SEMEN STUDY

The correlation of the semen findings and the histological pattern of the biopsy was as follows:

Of 76 patients with oligozoospermia, the biopsy and semen specimen examinations agreed in 66 or 87 per cent. Of the 19 patients with azoospermia the biopsy and semen specimen examinations agreed in 13 or 68 per cent. In the group with oligozoospermia the discrepancy in 13 per cent of the cases does not represent a percentage of error in the interpretation of the biopsy or semen findings. These cases, we believe are instances of oligozoospermia with normal spermatogenesis in whom the lesion is confined to the ejaculatory ducts and is obstructive in nature. They are always associated with prostatic and seminal vesicular infection. The semen is reduced in volume, contains a large number of pus cells, and the spermatozoa display relatively normal morphology. In the group with azoospermia the disagreement in 32 per cent is, of course, confined to those cases in which spermatogenesis is normal and in which the obstructive lesion in most cases, is more apparent. Of the 6 cases, 4 had bilateral obstruction of the epididymis and 2 had complete obstruction of the ejaculatory ducts with azospermia.

EVALUATION

When this study was begun it was hoped that a careful analysis of the testicular biopsy

sies would lead to a correlation between histological findings and specific etiological factors. It soon became apparent, however, that the pathological changes observed in the biopsies had no specific relation to the causative agent. It was found, moreover, that the presence or absence of peritubular fibrosis was a most valuable differentiating finding. Thus, no fibrosis was found in any of the clinical entities associated with underdevelopment of the testes, such as in the pituitary-gonadal deficiencies, in primary hypogonadism, and in cryptorchidism. Such testes uniformly showed tubules smaller in size than normal and lined by incompletely developed or undifferentiated epithelial elements. On the other hand, the acquired degenerative lesions, such as those due to toxins, inflammations or postpubertal endocrine disturbances, almost invariably showed some degree of peritubular fibrosis. The only exceptions apparently occurred in the mild cases of tubular degeneration, and in the very acute instances which did not, therefore, represent end stages. An example of the latter is the injury produced by stilbestrol (Case 3). Such cases are especially interesting in that they illustrate clearly the regenerative potentialities of the testes, when the toxic agent is removed or a stimulating remedy is introduced. The authors believe that if the stilbestrol had been administered over a sufficiently long period of time, tubular damage would have become so extensive that shrinkage would have occurred, generalized replacement fibrosis would have set in and regeneration would have been much less in evidence. As a matter of fact some parts of the section showed areas of focal fibrosis.

The evidences of tubular degeneration induced by the administration of both stilbestrol and testosterone propionate in our cases are fairly conclusive. It is clinical confirmation of the findings of several investigators who demonstrated tubular degeneration following the administration of a variety of androgens in the experimental animal. It is especially significant that in our case the testosterone propionate produced degeneration of the seminiferous tubules in a hypogonad, one in whom male sex hormone therapy is indicated according to our present concepts.

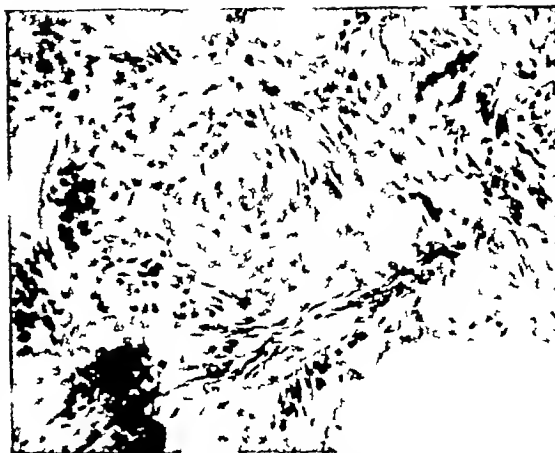


Fig 10. Case 6. Section from left testis showing destruction of tubules with replacement fibrosis ($\times 150$)

One point that deserves re-emphasis is that the pathological process in any testis is fairly uniform throughout and that a small specimen removed at biopsy is almost invariably representative of the entire testis. It is not uncommon, however, to find different degrees of involvement in the two testes even though the etiological agent is identical in each case. An example of this is the patient in Case 6, in whom the left testis was almost completely fibrosed, as demonstrated by biopsy, while the right one was severely and irreparably damaged by fibrosis of similar etiology but was still sufficiently spared to produce the spermatozoa found in the semen. It is interesting to note, however, that this patient's semen contained 58 per cent abnormally shaped spermatozoa.

It has not been sufficiently stressed that the majority of males with reduced fertility who are almost routinely treated with some type of endocrine product, do not show any clinical evidence of endocrine disturbance. Nor do these patients show any evidences of endocrinopathy when studied by the available laboratory procedures, such as basal metabolic rate, roentgenogram of the sella turcica, and urinary and blood levels of androgens and gonadotropins. There is, moreover, no logical justification for concluding that these patients have an isolated endocrine dysfunction of the seminiferous tubules. The observations in the present series of 95 testicular biopsies lend

additional support to the contention that the great majority of these testicular lesions are degenerative and are for the most part, due to local or distant inflammatory or toxic processes. Since no endocrine imbalance exists, such seminiferous tubules cannot be expected to respond to endocrine therapy.

It is not possible at the present time to determine the specific etiology of the lesions in the seminiferous tubules. Since most of the inflammatory and degenerative changes occur insidiously, the characteristic signs and symptoms of inflammation are lacking and the patient usually gives no history of such a complication (see Case 3). It may be pointed out moreover that these nonendocrine degenerative changes have been recognized before in autopsy material and have been reported upon by a considerable number of investigators. Berberich and Jaffe report degenerative lesions involving the seminiferous tubules in a large percentage of men who contracted a great variety of acute infections. Oberdorfer reports degeneration of seminiferous tubules in every German soldier dying of influenza in 1918 whom he examined at autopsy. He stresses an important concept with which we are in complete agreement, namely that almost all inflammatory lesions involving the seminiferous tubules begin in the epithelial structure of the tubules and that the peritubular fibrosis, though prominent is always secondary and indicates epithelial damage as well. A large variety of diseases may produce hematogenous lesions. Some of these provocative ailments are typhoid, paratyphoid mumps, diphtheria, scarlet fever, variola, influenza, typhus fever, tonsillitis, glanders, pneumonia, malaria, gout, rheumatic fever, furunculosis, osteomyelitis, cholecystitis, appendicitis, and localized focal infections with pyrogenic organisms.

SUMMARY AND CONCLUSIONS

1. Testicular biopsy is an innocuous procedure no more disabling than a Rubin test in the female, and should be established as a routine procedure in the study of male infertility.

2. The failure of tubular development is indicated histologically by the presence of small tubules which are filled with undifferentiated cell forms. Peritubular fibrosis is not present.

3. Degenerative lesions, if acute are recognized in testicular biopsies by the presence of necrosis and desquamation of the tubular epithelium. If the lesions are of long standing peritubular fibrosis is a distinct feature and signifies either the end stage of an inflammatory process or the replacement fibrosis which results as a consequence of shrinkage of the tubules.

4. The presence of peritubular fibrosis suggests severe damage to the youngest epithelial cells of the tubules probably affecting their regenerative potentialities.

5. The administration of sex hormones, either stilbestrol or testosterone propionate, induces tubular degeneration both in the hypersexual male and in the hypogonad.

6. The majority of male patients with relative infertility have no endocrine disturbances. Their semen deficiencies are the result of degenerative lesions of the seminiferous tubules caused by either regional or constitutional inflammatory or toxic processes. Endocrine therapy is not indicated in such instances.

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SOME MODIFICATIONS ON THE ASEPTIC DOUBLE VALVED TUBOGASTROSTOMY

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SINCE the publication of a former paper entitled "A New Aseptic Double-Valved Tubogastrostomy" I have had many opportunities to observe and to study the technique employed by various surgeons who have been kind enough to try this method. Often it was noted that, when placing the pursestring suture around the base of the diverticulum which was formed by traction on the anterior wall of the stomach, the operator attempted to make a perfect circle. In other instances the surgeon needlessly ligated gastric vessels and cut into the gastrocolic ligament to mobilize part of the greater curvature and even the posterior wall of the stomach so as to achieve such a circular pursestring suture in the seromuscular layer. Indeed, the diagrammatic sketch in my earlier paper did illustrate a circular stitch, but I have since learned by further experience that an irregular circular or even an oval shaped pursestring suture, when tensed finally to the proper degree of constriction, forms a diverticulum which is entirely satisfactory. This modification of my method, made possible because of the elasticity of the stomach wall, eliminates the necessity of infringing upon the gastric vessels at the greater and lesser curvatures. Before the second pursestring suture is applied in the creation of this diverticulum, the Babcock forceps is released and reapplied to the point selected as the final apex.

It is obvious that when the operator tenses the pursestring suture the stomach wall nearest to the sliding knot suffers the greatest amount of tension and constriction. This is avoided by introducing a pursestring suture which is "back stitched" after every fourth stitch is tensed until the base of the diverticulum is completely encircled. This precaution imparts relatively equal tension and constriction to all points and prevents undue crushing at any one point.

Numerous requests have been received by me to explain why I chose to include 2 valves in the tubogastrostomy. During the development of the technique it was found that food settling along the greater curvature and exerting a downward pull rendered the first valve slightly incompetent.

Therefore, a second valve was introduced, distal to the first, and was found to be unaffected by the weight of the feeding. However, in those instances in which there is not enough stomach wall to make a diverticulum that would permit the formation of 2 valves, a method which includes but one valve has been developed and tried by me and it has proved competent in preventing leakage of the gastric content, both in animal experiments and on human subjects. The technique of producing an aseptic tubogastrostomy with such a single valve is as follows:

- 1 With a Babcock forceps, traction is applied upward until the stomach wall is converted into a cone shaped diverticulum.

- 2 A pursestring suture—of braided silk, or No. 2 chromic catgut—is carried through the seromuscular layer at the base of the diverticulum in the manner indicated in Figure 1, A.

- 3 The Babcock forceps is released and reapplied to a final apical point on the diverticulum, and a second re-enforcing pursestring suture is inserted about 4 millimeters above the first (Fig. 1, B). (In a personal communication, L. Aries suggested placing the second pursestring suture midway between the first and third.)

- 4 Then a third pursestring suture is inserted about 1 centimeter above or peripheral to the second.

- 5 Lembert stitches are now placed in the seromuscular layer at right angles to all pursestring sutures (Fig. 1, C) in sufficient numbers to encircle adequately the base of the partially constricted diverticulum. The Lembert stitch employed here is somewhat modified, that is, the suture is inserted about 8 millimeters below the first pursestring and carried to a point about 1.5 centimeters beyond the second.

- 6 Interrupted seromuscular sutures are inserted in the anterior wall of the stomach at points superior, inferior, and lateral to the base of the tubal projection in order to fix the stomach wall to the peritoneum and posterior rectus sheath (Figs. 2 D and F). In a similar manner the tube itself is attached to the anterior rectus sheath.

- 7 An opening into the apex of the tube by means of cauterization may be made any time from the

additional support to the contention that the great majority of these testicular lesions are degenerative and are for the most part due to local or distant inflammatory or toxic processes. Since no endocrine imbalance exists such seminiferous tubules cannot be expected to respond to endocrine therapy.

It is not possible at the present time to determine the specific etiology of the lesions in the seminiferous tubules. Since most of the inflammatory and degenerative changes occur insidiously, the characteristic signs and symptoms of inflammation are lacking and the patient usually gives no history of such a complication (see Case 3). It may be pointed out moreover that these nonendocrine degenerative changes have been recognized before in autopsy material and have been reported upon by a considerable number of investigators. Berberich and Jaffe report degenerative lesions involving the seminiferous tubules in a large percentage of men who contracted a great variety of acute infections. Oberdorfer reports degeneration of seminiferous tubules in every German soldier dying of influenza in 1918 whom he examined at autopsy. He stresses an important concept with which we are in complete agreement, namely, that all the most all inflammatory lesions involving the seminiferous tubules begin in the epithelial structure of the tubules and that the peritubular fibrosis, though prominent is always secondary and indicates epithelial damage as well. A large variety of diseases may produce hematogenous lesions. Some of these probative ailments are typhoid paratyphoid, mumps, diphtheria, scarlet fever, variola, influenza, typhus fever, tonsillitis, glanders, pneumonia, malaria, gout, rheumatic fever, furunculosis, osteomyelitis, cholecystitis, appendicitis, and localized focal infections with pyogenic organisms.

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farthest from the site of lesion, that is, as far from the cardia as possible without encroaching upon the pylorus. The rationale guiding here is based on the assumption that the farther removed the gastrostomy site is from the malignancy, the longer it will take for the cancer cells to spread via a contiguous route to the tubogastric mouth and involve its lumen. In those few instances of carcinoma involving the lower third of the esophagus as well as the cardia and fundus of the stomach, the procedure of choice is jejunostomy.

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NINE YEARS' CLINICAL EXPERIENCE WITH STEEL WIRE AS A SUTURE MATERIAL

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OPERATIVE success depends upon mechanical technique, asepsis, and wound healing and despite the advances in laboratory and clinical research, little progress has been made in understanding or improving this latter fundamental operative requisite. While the necessity for anatomical reapposition and a minimum of trauma has been stressed, these requirements in many instances are imperfectly practiced. In the utilization of sutures and ligatures, the advance has been particularly slow. Such important matters as the selection of sutures have been left to the hospital purchaser, and the note on the operation sheet "routine abdominal closure" is an admission of content to follow out-dated and traumatizing methods of ligation and wound suturing. The publication of 126 articles on sutures and ligatures in the last 3 years is a more encouraging indication of the awakening to the responsibility for this important portion of the operation.

Ligating and suturing necessarily are as old as surgery. Not only were nonabsorbable sutures used, but catgut was described by the Arabian Rhazes, who wrote in 900 A.D. of the stitching of wounds with strips of sheep in-

testines. We know that Galen used catgut in addition to other sutures, but it was 1816 before Physick demonstrated the absorbability of this material. With Lister's discovery of the way to sterilize catgut, in 1869, this suturing material became the popular one. The strands were heavy and the needles traumatic, and even such a technician as Kocher reported an infection incidence of 70 to 80 per cent with this suture material. These infections led to his adoption of the silk suture which Halsted popularized after observation of Kocher's experience with the silk suture technique. This silk suture school has persisted in many places to this time. With the advent of the so called modern surgery, where stress was placed upon speed, catgut had a rebirth, and it has remained the most widely used suture material to this day.

At the Babcock Clinic in Philadelphia, dissatisfaction with the serum collections in clean wounds so often manifested after closure with catgut, stimulated an effort to find a more satisfactory suture material. From 1931 to 1935, such materials as cotton, linen, silk, Japanese and American fishline, silver and copper wires were utilized with varying success. Silk in the clean cases, in which the necessary finer instruments and technique were employed, was

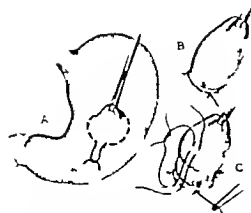


Fig. 1. A. Formation of cone shaped diverticulum from the anterior wall of the stomach by upward traction with Balfour forceps. B. Fixation of the formed diverticulum by basal pursestring sutures. C. Insertion of third pursestring suture about centimeter above or peripheral to the second. Lambert stitches are placed in seromuscular layer at right angles to pursestring sutures.

first to the tenth day after the completion of the operation (Fig. 3, G). It has been found more desirable to delay the opening as long as possible, depending upon the patient's ability to swallow

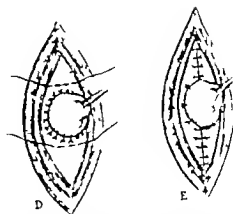


Fig. 2. D. Anchoring the anterior stomach wall to the peritoneum and posterior rectus sheath. E. The diverticulum protruding through the opening during the closure of the peritoneum and posterior rectus sheath. Additional interrupted silk sutures are shown anchoring the lateral sides of the stomach to the peritoneum and posterior rectus sheath.

liquid food, since a greater time is allotted for adhesions to form and for edema to disappear. This step culminates an operative procedure that requires a minimum of time and trauma and that is aseptic throughout.

In Figure 3 H a diagrammatic cross section illustrates the arrangement of the various layers of the stomach wall after the invagination resulting from the three pursestrings has been completed. It will be noted that while the modified Lambert suture invaginates the three pursestring sutures, it also produces a more abundant overlapping of mucosal folds within the tubal structure which are more than adequate in maintaining competent closure. Although the gastrotomy possessing only one valve has proved competent and is preferred by O'Donoghue, Aries, and others, I still favor my original double valued tubogastrostomy whenever an adequate amount of stomach wall is present.

At this point I would like to add a few remarks regarding the selection of the ideal site of the gastrotomy. In cases of carcinoma of the upper or the middle third of the esophagus, the operator may proceed to perform gastrotomy in any suitable portion of the anterior wall of the stomach. But in cases in which the malignancy involves the lower third of the esophagus or the cardiac portion of the stomach, the operator prefers to utilize that portion of the anterior stomach wall

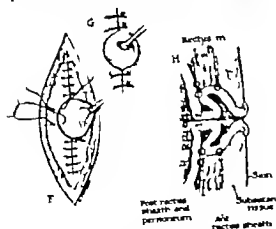


Fig. 3. F. Two united sutures are shown anchoring the tube proper to the anterior rectus sheath. Interrupted silk sutures are employed to close the split anterior rectus sheath. G. Illustrates cautery applied to the apex of the sheath. H. Diagrammatic cross section illustrating the broad tubular approximation of the basal wall. The circles represent suture ties employed throughout the operative procedure.

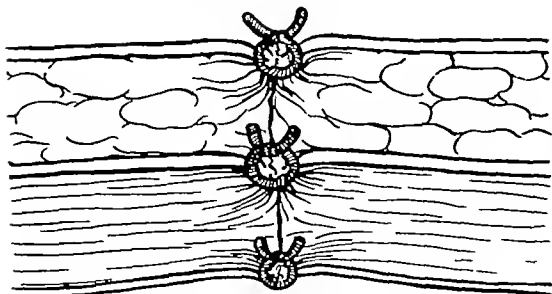


Fig 3a

Fig 3 a, Illustrates the frequent strangulation of tissues in the use of absorbable sutures, strands are heavy and the swelling causes more necrosis. Tissues should be lightly approximated—as shown in b, in which fine steel wire is used. c, Demonstrates tying technique—first knot is tied loosely and a half turn made to hold it. After square knot is complete the ends are cut short and turned under.

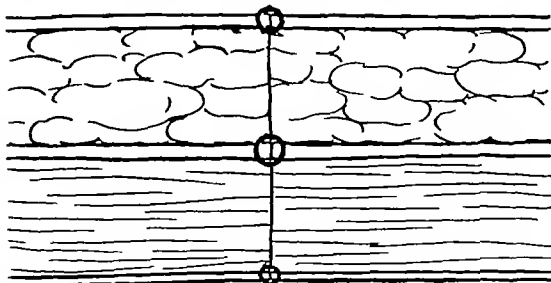


Fig 3b



Fig 3c

stances similar to those in which the sutures are to be used. Preparations and solutions or suspensions of the suture material have the disadvantage of presenting the material to the host in an unnatural fashion. Sutures, them-

selves, inserted in the human exactly as they will be presented in the wound closures, is the ideal way to test for the body's response to these foreign materials.

The author, under Dr Babcock's directions, implanted some 750 sutures of different materials in surgically prepared areas in 125 patients to learn the reaction of the patients to these materials. Sutures of plain No 1 catgut, chromic No 1 catgut, silkworm gut, alloy steel wire, silver wire dermal, and various types of fishline were inserted through the skin in different areas of the surgically prepared field and gross, bacteriological, and at times pathological observations were made, at 5 day, 7 day, 10 day, and 14 day intervals. The report of this work has been published previously (Babcock, 1935) but in every in-



Fig 4 Compound fracture of tibia and fibula with large skin defect. Previous fracture had occurred at same site and 14 operations had been done for osteomyelitis of this leg. Bone union was effected and a skin graft applied. Wire sutures only were used.



Fig 5 Steel wire which was removed after 4 months in compound fracture tibia and fibula. Notice how shiny and noncorroded the sutures are. Bone union was complete.



Fig. 1. Plastic for pendulous hypertrophied breasts which reached 4 inches below umbilicus. All sutures were

of steel wire. Right, photograph taken 6 months after bilateral operation.

satisfactory. In other instances, in which sepsis was present, the resulting sinuses made it most undesirable. The fishline, like catgut and some cotton, would absorb fluid, lengthen and swell with inevitable tensile weakening. Silver wire so admirably employed by Sims in his closures of vesicovaginal fistulas, had the disadvantage of breaking on the knot and its oxidation subcutaneously left a discoloration.

In 1933 the first alloy steel wire was employed at the Babcock Clinic and a thorough

investigation and clinical study were made. In reviewing the work on suture experiments one is confronted with the conflicting reports based on results of nearly identical investigations. These studies were based on animal work. Although animal experimentations are necessary the results are frequently fallacious, and pro and con interpretations may be made at times from the same results. It is our contention that experiments to demonstrate sensitization and allergic manifestations to sutures should be conducted under circum-



Fig. 3. Sternum repair and plastic removal of large apron of fat after weight reduction. All sutures were of steel wire. Right, primary healing took place despite wound site near area of contamination.

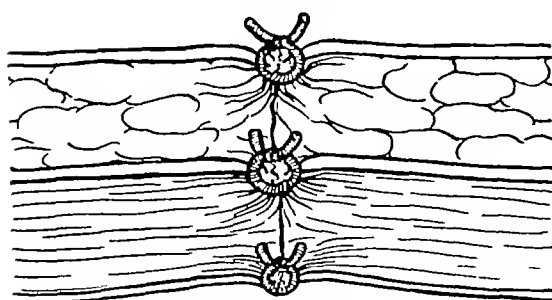


Fig 3a

Fig 3 a, Illustrates the frequent strangulation of tissues in the use of absorbable sutures, strands are heavy and the swelling causes more necrosis. Tissues should be lightly approximated—as shown in b, in which fine steel wire is used. c, Demonstrates tying technique—first knot is tied loosely and a half turn made to hold it. After square knot is complete the ends are cut short and turned under.

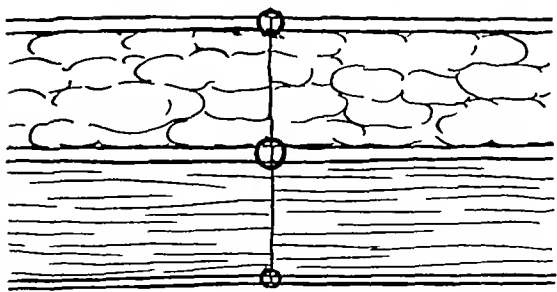


Fig 3b



Fig 3c

stances similar to those in which the sutures are to be used. Preparations and solutions or suspensions of the suture material have the disadvantage of presenting the material to the host in an unnatural fashion. Sutures, them-

selves, inserted in the human exactly as they will be presented in the wound closures, is the ideal way to test for the body's response to these foreign materials.

The author, under Dr Babcock's directions, implanted some 750 sutures of different materials in surgically prepared areas in 125 patients to learn the reaction of the patients to these materials. Sutures of plain No. 1 catgut, chromic No. 1 catgut, silkworm gut, alloy steel wire, silver wire dermal, and various types of fishline were inserted through the skin in different areas of the surgically prepared field and gross, bacteriological, and at times pathological observations were made, at 5 day, 7 day, 10 day, and 14 day intervals. The report of this work has been published previously (Babcock, 1935) but in every in-



Fig 4. Compound fracture of tibia and fibula with large skin defect. Previous fracture had occurred at same site and 14 operations had been done for osteomyelitis of this leg. Bone union was effected and a skin graft applied. Wire sutures only were used.



Fig 5. Steel wire which was removed after 4 months in compound fracture tibia and fibula. Notice how shiny and noncorroded the sutures are. Bone union was complete.



Fig 6 Photomicrograph of fascia with steel wire 4 years after insertion in central hernia repair. There is no tissue reaction to suture material. $\times 45$

stance in which catgut was used a reaction varying from a flare to a distinct pustular response was noted. Silk was variable in its



Fig 7 Wound seven days after operation for ruptured appendix and closure with steel wire. While there has been drainage the suture areas are clean and nonirritated.

response but at the end of 10 days in over 50 per cent there was some necrosis surrounding the suture. Wire gave the least reaction and the steel without the skin discoloration due to the oxidation of the silver wire, was quite imperceptible in 95 per cent of the cases. In the last year a second series of experiments on patients have been performed. Four suture materials, chronic catgut, silkworm gut, silk, and steel wire have been placed near clean surgical wounds. Each strand has been passed



Fig 8 Roentgenogram of multiple steel wire sutures buried in fascia in hernia repair.



Fig 9 High amputation for obliterative vascular disease. Closure with steel wire. Primary union.

through the deep fascia, and the sutures have been subjected to a regulated strain at various intervals after operation. Results so similar to the experiments previously reported have been obtained that the previous work is collaborated.

The allergic factor in catgut has been subject to more study. The work of Kraissl, Kisten, and Cimotte was confirmation of the factor of allergy to catgut in wound healing. They reported disruption in 35.7 per cent of the abdominal wounds in guinea pigs previously immunized with catgut and a sensitivity reaction to catgut in 332 humans. Hinton's findings that 9 of 112 patients who had had a previous operation were sensitive to fresh sheep gut (0.8 per cent solution) is further confirmation of the part reaction may play in the various stages of dehiscence. Taylor's report that catgut is a culture medium has been confirmed many times, and Whipple was able to reduce his incidence of wound infections from 7.55 to 2.04 per cent by changing from catgut to silk.

It is obvious that the ideal suture material is one in which there is a minimum of trauma necessary to insert it, a tensile strength sufficient to assure its maintenance and the least possible tissue response to it. In our experience steel wire fulfills these requirements more satisfactorily than any other suture at present available.

For the last 8 years, steel wire has been employed to exclusion by the author as retention and skin sutures with success in all abdominal as well as other wounds. It has been buried in the closure of fascia in inguinal and all ventral or incisional hernias. It has been particularly successful in the presence of sepsis and its efficiency has permitted primary closures in appendicitis with peritonitis, in colostomies after 1st stage Mikulicz operation and in fistulas. It has replaced all other sutures in plastic operations (Figs 1 and 2).

As in the use of silk, the technique must be varied. Small bites of tissue should be taken (as shown by Preston's experiments) and smaller needles and finer instruments with less trauma are utilized. Tissues must be merely approximated, without pulling the knot tightly, as the steel wire will not give

with tissue swelling. A square knot should be tied and the ends cut on the knot (see Fig 3). The surgical nurse must prevent kinking of the wire during its preparation and the first assistant can save valuable time by following the suture through to prevent a wire snarl. The wire should be of such size as to have only sufficient strength for the purpose for which it is being used. A No 36 or No 37 on the Sharpe and Smith gage is effective in the skin, while a No 33 or No 34 makes an ideal buried fascia suture. For heavy bone approximation a No 30 gauge is sufficient (see Figs 4 and 5). For the bowel, fine No 36 interrupted steel wire suture is well tolerated and especially effective on the serosal surfaces, will cause so little reaction that the tendency to adhesions and obstruction is minimized. Jones and his co-workers have confirmed the incidence of lowered infection by the use of wire in bowel work. His report of a reduction of infection in abdominal wounds after 116 cases of resection of the colon from 27.5 per cent in those in which catgut was used to 0.85 per cent in those cases in which alloy steel sutures were employed, is so significant that further comment on this work is unnecessary.

In this last year, during an operation for carcinoma of the cecum, an opportunity was presented to study steel wire buried in a ventral hernia closure 4 years previously. The fascial section and wire were excised, and not only were the sutures bright and shining, but the surrounding tissue showed neither gross nor microscopic evidence of tissue or foreign body response (Fig 6, $\times 45$).

In the 9 years that this suture material has been used, we have never seen tissue reaction to it. In a few instances in which overenthusiastic residents have squeezed the wound edges by ligating the sutures too tightly, a local necrosis has developed, due to constricting avascularity. In an analysis of the last 145 appendix operations in which 75 were of the acute, gangrenous type, all closed with the steel wire, there has been wound edge infection in only one. Figure 7 shows the abdominal wound 7 days after removal of a ruptured gangrenous appendix. While there has been drainage, it has been between the

sutures which are still *in situ* and no reaction has occurred around them, nor has there been wound breakdown.

In 85 inguinal hernioplasties, steel wire has been used to close the layers from the peritoneum, while in all recurrent inguinal and ventral hernias the wire has been buried in the fascia. Experience with wire as the only suture in hernias has led to its adoption for even suturing the base of the sac and transplanting the base under the rectus muscle. An x-ray film shows buried steel wire in the fascia of a large ventral hernia 4 years after operation. Sutures were of No. 34 alloy steel wire, and the wound healed primarily (Fig 8). There has been but one recurrence and this was in a ventral hernioplasty in an elderly individual with bronchiectasis who had had 2 recurrences before and who coughed his hernia out in the first 48 hours. In these hernias we believe that wire plays a most important part and in our hands is much more satisfactory than such foreign materials as silk, kangaroo tendon, or the routine fascial transplants. The fascial sutures require such traumatic needles and large openings that it is surprising not to observe some with recurrence due to needle apertures alone.

In major amputations for vascular disease when only steel wire has been used in closure, we have had 92.3 per cent primary unions in the last 3 years, 26 cases. Figure 9 demonstrates how primary healing is obtained even in high amputations with the steel wire. The stump is in an easily contaminated area, but healed satisfactorily. Previous experience with other suture materials was not satisfactory.

The wound after ligation of the saphenous vein at the fossa ovalis has been approximated with the wire and the infections so prevalent in this area when we used silk have been reduced to 8 in the last 150 patients.

With many others we have felt that wound disruption or avulsion is most often due to inadequate postoperative support, rather than the type of operation, a predilection or autonomous suture destruction. At one time we saw three avulsions on a surgical service in a

month following the routine adoption of Montgomery strings instead of adhesive strap support. The incidence of diathesis is greatest at the time of retention suture removal. Prior to burying the wire fascia sutures it had been our practice to retain the retention sutures *in situ* for a long time and even to permit patients to leave the hospital with the sutures in place. This was easily handled as one felt safe in doing this with the steel wire as no suture abscesses will be formed. In more than 500 major abdominal operations there has not been a wound disruption. In one instance in which a double barrelled colostomy after a 3 stage Mikulicz operation for carcinoma of the hepatic flexure was closed primarily with the steel wire only the patient returned 2 years later complaining that she felt a wire suture. Examination showed one of the wires had become unknotted and its tip was presenting at the skin edge. Its removal was simple and this patient has had no other complaints in 5 years of observation.

SUMMARY

Nine years clinical observation has confirmed experimental work showing less tissue reaction to steel wire sutures. It is effective in abdominal closures in which it may be used as a buried suture and, in infected or contaminated areas, it is particularly indicated. A finer technique and approximation without strangulation is necessary in its use. It has been adopted to exclusion in all hernias and markedly reduced the morbidity and the disability time. Patients so sutured may be returned to industrial work in 4 weeks rather than the routine 8.

Its wide use in intestinal anastomoses, as the areolar sutures and in the plastic surgery field is stressed.

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A STUDY OF THE EFFECT OF MORPHINE, ATROPINE, AND SCOPOLAMINE ON THE BRONCHI

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THIS study is concerned with the effect upon the tracheobronchial tree of the commonly prescribed drugs or combination of drugs, for premedication to anesthesia, and with morphine, the drug most commonly used for postoperative relief of pain. The drugs studied were morphine sulfate, $\frac{1}{4}$ grain, atropine sulfate, $\frac{1}{50}$ grain, scopolamine hydrobromide, $\frac{1}{100}$ grain, morphine sulfate, $\frac{1}{4}$ grain, and atropine sulfate, $\frac{1}{50}$ grain, morphine sulfate, $\frac{1}{4}$ grain and scopolamine hydrobromide, $\frac{1}{100}$ grain.

There has been considerable speculation and controversy over the mode of action of these drugs on the bronchi and in what manner they affect the bronchial secretions which are brought to the oropharynx. Certainly, opinions on the subject vary among clinicians. This difference of opinion may be due to the fact that conclusions are drawn from infrequent clinical observations rather than laboratory or clinical experiments.

Waters and others, in studying these drugs demonstrated that in so far as their effect upon respiration, circulation, blood pressure, tidal exchange, minute volume exchange, and nausea and vomiting was concerned, the combination of morphine and scopolamine was the most satisfactory. They also showed that the most marked depression in respiration and circulation occurred $\frac{1}{2}$ to 2 hours after administration of these drugs.

On the basis of our studies and clinical observations both the surgical and anesthesia departments of the Wisconsin General Hospital have concluded that the combination of morphine and scopolamine in individualized doses in the ratio of 25:1 has the least depressant effect upon the raising of bronchial secretions and the suppression of cough reflex.

In order to obtain some definite data on this subject a clinical experiment was carried out on a young white female who presented a bronchopleurocutaneous fistula. Her case history follows.

White female aged 18 years was admitted to the Wisconsin General Hospital on May 20, 1940, with the chief complaint of "lung abscess." Following a fourth operation in 1938 for intestinal obstruction, she developed a left lower lobe lung abscess. She was treated in two other clinics before her admission. The treatment had been conservative, consisting of inadequate postural drainage, bronchoscopic aspirations, bed rest, diet, and "tonics." Her progress was unsatisfactory, and she was referred to this hospital. Her complaints on admission were as before, namely, intermittent fever, cough with the raising of sputum, hemoptysis, weakness, and weight loss.

On admission her temperature was 101.8 degrees, and the patient appeared toxic, undernourished, and chronically ill. Physical findings were consistent with a left lower lobe lung abscess. X ray studies revealed bronchiectasis, atelectasis, and encapsulated fluid in the left lower lobe. X ray also revealed a chronic pansinusitis.

In view of the inadequate conservative treatment previously, the patient was again given a trial on postural drainage, which resulted in no improvement. Therefore, on June 27, 1940, cauterization of the lung abscess was instituted. Multiple small abscess cavities were encountered and aspirated, and a pack was inserted. On the seventh postoperative day the pack was removed, and a large abscess cavity with many bronchopleurocutaneous fistulas was noted. Following this her condition improved rapidly. She gained 50 pounds in weight in 6 months. No cough, sputum, fever, or abnormal blood counts persisted at the time of discharge. A large bronchopleurocutaneous fistula was still present.

METHOD

The experimentation was not begun until the patient's sputum and cough were gone and she was gaining weight. After the experiment was completed, lipiodol was instilled, both through the fistula used for the experiment and from above through the trachea, and the diagnosis of bronchiectasis of the left lower lobe was confirmed. The lipiodol which was instilled through the bronchopleurocutaneous fistula was seen to enter a relatively large bronchus in the left lower lobe.

All of the data for this experiment were obtained by the same operator so that the technique followed was uniform. An easily accessible, fairly large bronchial opening (a bronchopleurocutaneous fistula) was selected and used throughout.

Powdered carmine dye was deposited by means of a small eye curette into this same bronchial opening. Carmine dye was used because of its insolubility and lack of absorption in body secretion and because it is nonirritating. Its bright color made it easily detectable in small amounts. The dye was deposited just within the bronchial opening during ordinary inspiration with the patient

TABLE I.—EFFECT OF DRUGS ON APPEARANCE TIME OF CARMINE DYE

Drugs and dosages	Number of trials	Average time interval between onset of drug and dye-tosses	Average appearance time—minutes	Percentage change from control time of 8.66 minutes*
Morphine gr 1/4				
Morphine gr 1/2			8.48	+7.0
Morphine gr 3/4				+7.0
Atropine gr 1/100				+3.8
Atropine gr 1/50		14	8	+33
Scopolamine gr. 1/100		14		+18.6
Scopolamine gr. 1/50		14	8	
Morphine gr 1/4 Scopolamine gr. 1/100	8	14		+6.2
Morphine gr 1/4 Atropine gr. 1/50		5	17.8	+109

*The positive percentage indicates the increased time. In negative percentages indicates decreased appearance time.

on her right side. It was deposited during inspiration because the expiratory blow from the bronchial opening was sufficient to blow the fine powder from the cigarette, thus making it impossible to get any of the dye into the bronchus. It was appreciated that the height to which the dye was inspired was variable but it was sufficiently uniform so that the ranges of the control "appearance times" were uniform.

The dye was deposited 1/2 to 2 hours after the hypodermic injection of the drug being studied. The reason for the selection of this time interval is that Waters and others have shown that the maximum effect of these drugs is secured between 1/2 to 2 hours after their administration hypodermically.

The patient remained on her right side after the dye had been deposited. The time of deposition was noted and recorded. A third person sat at the bedside and recorded the first appearance of the dye in the sputum. The patient was intelligent and co-operative throughout the period of the experimentation. She did not cough until she got the stimulus to cough, i. e. until the cough reflex was stimulated by the foreign particles. The dye almost invariably appeared with the first cough. After two to three consecutive coughs the stimulus was gone. No more dye appeared even though she coughed later in the day. The time between the deposition of the dye and its first appearance in the sputum will henceforth be called the appearance time.

Only one trial was performed a day in order to avoid cumulative effect of the drug, and often one

day or more was allowed between trials to avoid addiction to the morphine. The patient did not know what the medication was nor what its effect should be.

Before the controls to this experiment were performed, many daily carmine dye instillations with out medication were done until it was determined that the results were uniform. At this point it was decided that the effects of the acute infection and of the surgery upon the bronchial tree were past and that the results were due to normal action of the bronchi themselves. A subsequent left lobectomy and pathological study showed bronchi with normal cilia. During the course of experimentation the sputum was at a minimum and there was no drainage from the bronchial opening.

RESULTS

It was found that the position assumed by the patient made no difference in the appearance time of the carmine dye. Trials with the patient on her right side, on her left side on her back, and in the sitting position gave comparable results. Because of the ease with which this experimentation could be done with the patient on her right side this position was chosen as the one of choice for the trials.

Fifteen control instillations, without medication, were performed. The average appearance time (that is the time elapsing between the instillations of the carmine dye and the dye appearing in the sputum) was 8.66 minutes. Controls were performed also during and after the trials with medication, and it was found that the control times remained uniform.

The drugs were then tested in the dosages as given, and the percentage change from the control time of 8.66 minutes was calculated, as shown in Table I.

The question, of course, then arose as to how long these drugs exerted their effect. Attempts at repeated dye injections were then tried. It was found that the experiment could satisfactorily be carried out for only a period of 3 hours. The results of these trials appear in Table II.

EVALUATION

The function of raising secretions or small foreign particles from the bronchi probably depends locally on three separate actions, namely: (1) the character of the bronchial secretions, (2) the action of the bronchial cilia, and (3) the cough reflex. Any variation from normal in any one of the actions may cause a deviation from normal in the appearance time.

It was realized at the outset that an experiment of this sort has many sources of error. These were minimized and eliminated wherever possible. We are not, therefore, interested in the actual appearance times, but rather in the "trend of change" as indicated by the percentage change over the normal control times, and the comparative amount of change caused by one type of medication as compared to the other. We feel sure that these results do indicate the trend of change and the comparative amount of change caused by these drugs on bronchial action.

Atropine and scopolamine themselves have little, if any, depressive action, but they do change, both objectively and subjectively, the character and amount of the secretions from the mucous glands. Whether they have any depressive or stimulating action on the cilia of the bronchi is not known. We do know that morphine causes a generalized depression of cellular metabolism and irritability. That it has a depressive action on certain respiratory functions has already been indicated (1, 2). It causes depression in the cough reflex. If morphine affects these ciliated cells as it affects most other cells of the body, we can rightly surmise that the ciliary action is also depressed.

With morphine alone the appearance time was increased 11.6 per cent over that of the control. The effect here was probably due to the generalized depressive effect, especially of the cough reflex and of ciliary action.

With atropine alone the appearance time was greatly increased, 36 per cent over the control, more so even than with the morphine alone. The cause of this perhaps lies mainly in the change in the amount and character of the bronchial secretions.

Scopolamine alone apparently had little effect. We know however that scopolamine does at least change the amount and character of the secretions, but in this experiment the change apparently was not sufficient to alter the appearance time noticeably.

When the combination of morphine and atropine was used, the change was more marked than with either drug alone, 107 per cent as compared with 11.6 per cent and 36 per cent. The appearance time was greatly prolonged. The drugs apparently here have a synergistic action, with all three of the factors, namely, bronchial cilia, cough reflex, and bronchial secretions, being altered to cause this increase in appearance time.

When morphine and scopolamine were given together, the appearance time was again greatly increased although the change was not as marked

TABLE II—EFFECTS OF DRUGS ON APPEARANCE TIMES AFTER 3 HOURS

Drug and dosages	Number of trials	Average time interval between giving of drug and of dye—hours	Average appearance time—minutes	Percentage of change from control time of 8.66 minutes
Morphine gr $\frac{3}{4}$ Atropine gr $\frac{1}{50}$	5	3	14.5	+91.8
Morphine gr $\frac{3}{4}$ Scopolamine gr $\frac{1}{100}$	4	3	11.0	+27.8

as appeared with the morphine and atropine together, 62.7 per cent as compared with 107 per cent. It was prolonged greatly as compared with either drug alone, 62.7 per cent as compared to 11.6 per cent and -2.3 per cent, and apparently their actions were again synergistic.

The results of the repeated dye injections show that the effects of the drugs are prolonged, in this case well over 3 hours from the time of giving the drugs—morphine-atropine combination 91.8 per cent over the control, and morphine-scopolamine combination 27.8 per cent over the control.

When comparing the relative effects of the morphine and atropine, and morphine and scopolamine, they bear out what we have always felt clinically at this hospital, but have never shown experimentally before, namely, that the morphine and scopolamine given in individualized doses (ratio here is 25 to 1) is a better preanesthetic combination than the former. The percentage change of morphine and atropine here over the control was almost twice that of the morphine and scopolamine.

SUMMARY

1 Morphine sulfate, atropine sulfate, and scopolamine hydrobromide were studied both alone and in combination, to determine their effect upon the bronchial tree, in a patient with a bronchopleurocutaneous fistula. The "appearance time" of the carmine dye was used as the method of testing the effect of drug action.

2 In 15 control experiments, the average appearance time of the dye was 8.66 minutes. The control time was checked during the course of the experiment and was found to be uniform.

3 Morphine sulfate caused an increase in the appearance time of 10 minutes, or a percentage change of 11.6 per cent over the control.

4 Atropine sulfate, 1/100 grain, caused an increase in the appearance time of 3.1 minutes, or 36 per cent over the control. Atropine sulfate, 1/50 grain, caused an increase in the appearance

time of 3.2 minutes, or 37.2 per cent change over the control.

5. Scopolamine hydrobromide caused a decrease in the appearance time of 0.2 minutes, or a 2.3 per cent, change over the control.

6. Morphine-atropine combination increased the appearance time 9.2 minutes, or a .07 per cent, change over the control.

7. Morphine-scopolamine combination increased the appearance time 5.4 minutes, or a 62.7 per cent, change over the control.

8. Three hours after the morphine-atropine had been given the appearance time was increased 5.9 minutes, or a 91.8 per cent change over the control.

9. Three hours after the morphine-scopolamine had been given the appearance time was increased 2.4 minutes, or a 27.8 per cent change over the control.

10. The sources of error in this type of experiment were appreciated. As a result the trend of change and the comparative amount of change of one medication as compared to another are the findings of importance in this study rather than the actual appearance times.

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A SIMPLE OPERATION FOR STABILIZATION OF THE KNEE JOINT

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AN operation for stabilization of loose knee joints following injury to the crucial ligaments is described herein. The operation is simple to perform, it does not necessitate opening of the knee joint, it eliminates the need of long postoperative immobilization, and it makes possible, and desirable, early walking with the aid of a knee cage.

Looseness of the knee joint as a result of injury to the crucial ligaments is a serious disability. Milch pointed out that injury to the crucial ligaments usually involves other supporting structures of the knee, particularly the internal lateral ligament when the anterior crucial has been traumatized. He believed that primary surgical treatment should be directed toward the repair of the internal lateral ligament rather than the cruciate. Bennett stated that a knee may be fairly stable in spite of severance of the anterior crucial ligament, provided that the internal lateral ligament is normal. According to Cubbins and his associates, early operation following complete dislocation of the knee is not indicated. They advised immobilization of the knee for 120 days, arguing that some knees so treated will recover.

The operation which Hey Groves (5, 6) described for the repair of torn crucial ligaments with fascia lata established the principles upon which most of the subsequent repairs have been based. A modification of the Hey Groves operation to include strengthening of the internal lateral ligament was later reported by Alwyn Smith. Fascial transplants, however, do not restore a knee to normal function after long continued disability due to injury of the collateral ligaments of the knee even though stabilization may be effective (9).

Less difficult procedures than those advocated by Hey Groves and Alwyn Smith have since been devised and have given satisfactory results. Bennett plicates the capsule and uses two parallel strips of fascia for further reinforcement (Fig 2, A). Cotton and Morrison draw a strip of fascia through holes drilled in the tibia and femur, crisscrossing the strip as it is pulled through the hole (Fig 2, B). Ryerson, has modified this procedure somewhat, he drills the holes in the tibia about $\frac{7}{8}$ inch apart, making the anterior

hole at a lower level, and ties a square knot in the fascial strip near the femur before he draws its long end through the tibia (Fig 2, C). D M and B M Bosworth implant a fascial strip in a tunnel in the posterior part of the tibia, draw it through another tunnel in the femoral epicondyle, then pass it through a tunnel in the anterior part of the tibia, and finally suture the fascial strip at the femoral epicondyle (Figs 2, D and 2, E). The Bosworths stated that when the external collateral ligament is repaired, the attachment may be made to the tibia and the head of the fibula.

The operation now reported is based on Testut's observation that movement of the knee joint is centered in the posterior portion of the femoral condyles. By superimposing roentgenograms

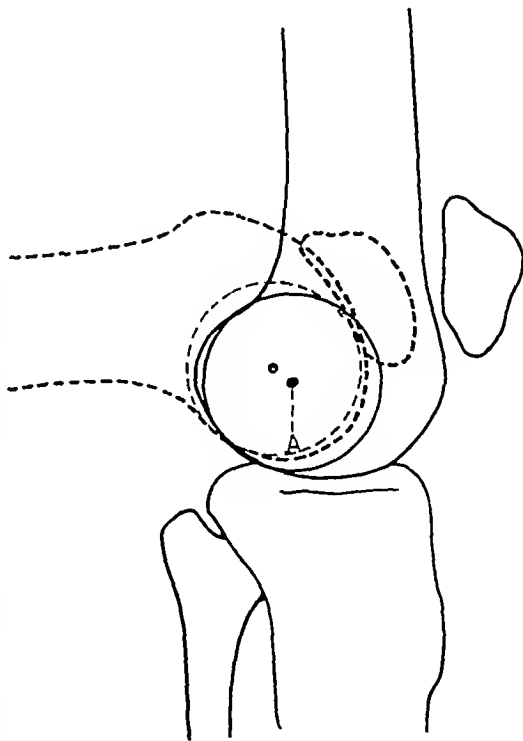


Fig 1 Schematic drawing of roentgenograms taken with the knee in complete extension and 90 degrees' flexion. A indicates nearly fixed point.

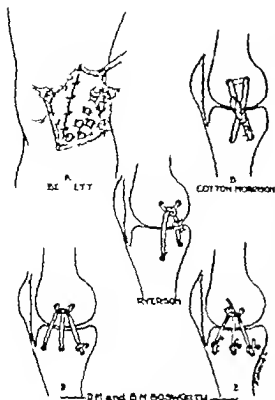


Fig. 2. Stabilization operations previously described in which the reinforcement is placed on the medial or lateral side of the knee.

taken with the knee in extension and at different angles of flexion, a nearly stationary point is localized in the center of the ring formed by the extension of the arc made by the posterior and inferior portions of the femoral condyles (Fig. 1). Theoretically this point does not change its distance from any fixed point in the tibia during flexion and extension of the knee joint. A strip of fascia applied so that it crosses the fixed point, as is done in the present operation, will therefore remain at the same degree of tension with the knee in extension and in any degree of flexion. Practically this arrangement of fascial strips has been successful since it has given good functional results under adverse conditions.

It has now been almost 10 years since I performed the first stabilization operation by the method now described. Up to the present time I have performed this operation on 10 patients.

Two patients who were re-examined in 1939, 8 years after the operation, reported that they had had no disability during this period. One was then employed as a truck driver although the industrial accident commission had paid him 60 per cent lost function of a leg 6 months after the operation. The other patient was working as a hook tender in a logging camp, and had been employed continuously at this arduous work since approximately a year following his operation. This patient had been awarded 45 per cent lost function of a leg 3 months following the operation.

OPERATIVE TECHNIQUE

A strip of fascia, approximately 12 inches long and 1 inch wide, is removed from the fascia lata of the contralateral extremity. A stripper is not used because it is difficult to obtain fascia of the proper width and length by this means. The fascia is cut into four strips, each of which measures approximately $\frac{3}{8}$ inch in width and 6 inches in length. The strips are tied into Gallie needles, and placed in a piece of gauze soaked in saline.

After the fascia has been prepared, an incision 6 inches long is made in the midline on the lateral side of the affected knee. A similar incision is also made on the medial side of the same knee. The skin and the superficial fascia are then dissected free from the deep fascia for a distance of 2 inches on either side of both incisions.

Lateral side (Fig. 3) The first fascial strip is placed in the insertion of the biceps muscle at the head of the fibula, and its lower end is secured in place by suturing it through itself. It is then carried obliquely forward to a position near the superior pole of the patella. Here the free end is passed deep into the tendinous expansion of the suprapatellar tendon, turned back on itself held tightly in place, and secured with a number of interrupted catgut sutures. The fascial strip does not penetrate the knee joint.

The second fascial strip is attached to the deep fascia on the anterolateral surface of the tibia. This strip is carried obliquely backward, crossing the first, and its free end is fastened securely to the fascia and some of the fibers of the biceps muscle. The two strips should cross on a level with the fixed point in the femoral condyle.

Medial side (Fig. 4) The third fascial strip is started as far back as the posteromedial border of the tibia, at about the same relative level as the head of the fibula and is buried deep in the fascia which in this region covers the tendons of the internal hamstring muscles. Some of the fibers of these tendons may be included in the suture. The fascial strip is then brought obliquely forward and

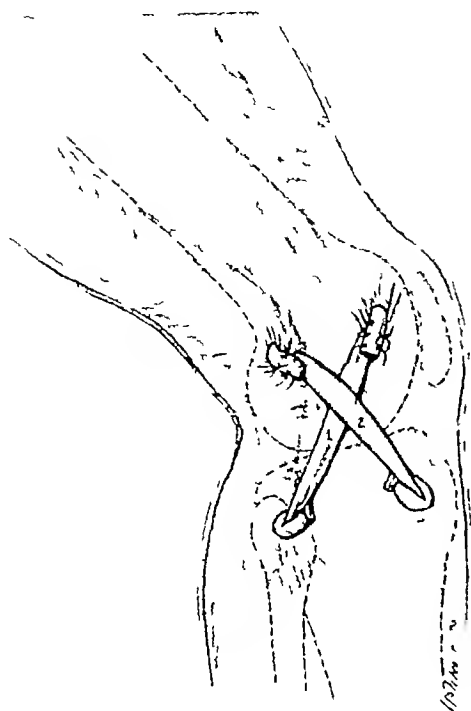


Fig. 3 Lateral view of the knee showing the order of placing the fascial strips, the method of their fixation, and the tension of the tissues after the fixation is completed

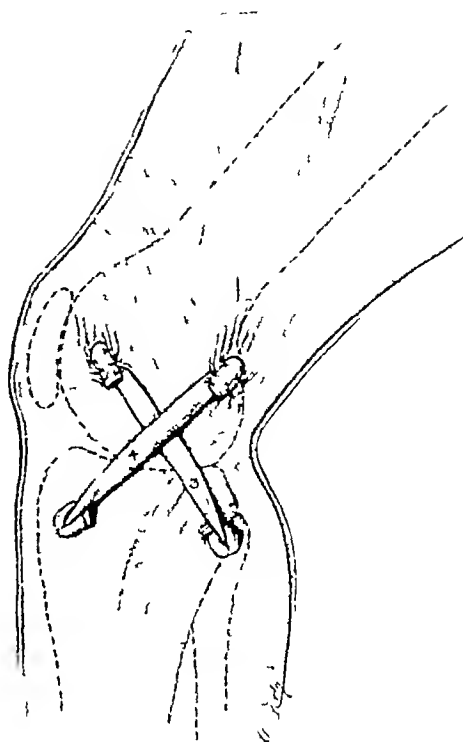


Fig. 4 Medial view of the knee showing the method of the placing of the 3rd and 4th crossed fascial strips in this region

upward, and its free end is inserted just medial to the superior pole of the patella

The fourth fascial strip is started at the same level, on the anteromedial border of the tibia. It is carried obliquely backward and upward, crossing the third strip, and is sutured to the fascia overlying the internal hamstrings. The suture may include some of the fibers of these muscles. These two fascial strips, like the first two, should cross on a level with the fixed point in the femoral condyle. When all the strips have been sutured into place, the first runs parallel to the third, and the second to the fourth.

No sutures are used except those of interrupted catgut which secure the fascial strips as described. The skin of each incision is usually closed with silk, and a compression dressing of sterilized cecil cotton¹ is applied.

When the skin stitches are removed, a non-padded walking cast, extending from the groin to,

and including, the toes of the affected extremity, is applied for 2 weeks (the postoperative care of the first 2 patients did not include the nonpadded cast). During the 2 weeks' period the patient is urged to bear some weight. At the end of this time, a long knee cage with 12 inch leather thigh and leg cuffs is supplied. The cage allows 10 degrees' flexion at the start. Flexion thereafter is gradually increased over a 2 or 3 months' period of time.

Abnormal mobility is present in the knee for some time after the operation. And often the hypermobility increases during the 4 to 5 weeks' period immediately following the operation. After this, however, the knee will begin to tighten. The patient is permitted to walk as he sees fit, and no limit is placed on his activities so long as he wears the brace with which he is supplied. Some of the patients have returned to work before this support was removed. The brace should be worn until the quadriceps muscles have developed and the hypermobility of the knee joint has decreased. Sometimes it is necessary to wear the knee cage for 5 or 6 months, or even longer.

¹Cecil cotton is a nonabsorbent bleached batting which comes in 8 ounce weight containing 50 per cent staple cotton and 50 per cent cotton linters and in 16 ounce weight containing 75 per cent staple cotton and 25 per cent mill run linters. A good grade of nonabsorbent bleached cotton batting would be just as satisfactory.

CASE REPORTS

CASE 1. L. D. male aged 37 years, as admitted to St. Vincent's hospital on December 6, 91 because of a knee injury in his right knee. He stated that he could feel the knee joint pop in and out during flexion, and that the knee dislocated back and laterally. This knee had been injured on February 6, 91, and in 31 y of that year the internal semitendinous cartilage had been removed.

On examination the patient as found to have torn posterior cruciate ligament. The knee joint as extremely lax.

The stabilization operation now reported as performed on December 8, 91. Three weeks later the patient as discharged from the hospital. At that time he as fitted with long knee cage which allowed approximately 10 degrees flexion of the knee. Six months after his discharge his claim with the industrial accident commission as closed with permanent partial disability and of 60 per cent.

This man as re-examined in 939, approximately 8 years after his operation. He as then employed as a truck driver. He had, however, first returned to his former work in the woods and had been able to continue it. During his work in the woods he had noticed that when he jumped from one log to another he usually slighted on the extremity which had not been operated upon. Nevertheless, few years later he had been able to take part in log rolling contest.

CASE 2. L. G. male aged 30 years, was admitted to St. Vincent's hospital on February 9, 912 complaining of a wobbles and abnormal motion of the right knee. He had sustained fracture of the right tibia in 912, the knee joint on January 23, 913.

On examination it as found that the right leg could easily be moved on the thigh both anteriorly and posteriorly. There as also some increase of mobility medially and laterally.

The stabilization operation as carried out on February 9, 912, and on March 9, 912, the patient left the hospital. The cast which had been placed on the extremity at the time of the operation was removed before the patient as discharged. After his discharge he as no support. On June 9, 912 his claim with the industrial accident commission as closed with permanent partial disability and equal to 45 per cent loss of function of leg.

This man as also re-examined approximately 5 years after his operation. At that time he stated that he had not been disabled by the knee, and that he never thinks about it any more. He had returned to his job as a book tender in logging camp about a year after the operation, and had been employed continuously since then. His work as arduous and dangerous, and necessitated pumping and moving about quickly on uneven ground.

CASE 3. J. H. male aged 45 years, had been injured on August 5, 917, when a large log rolled against the outer side of his lower right leg. A smaller log had struck the thigh on the inner side causing dislocation of the right knee. The dislocation had been reduced immediately and cast had been applied. Following this the patient had continued to be supported until November 5, 917.

Examination on January 3, 918, revealed instability of the right knee, some genu recurvatum, and weakness of the external lateral ligament. It as possible to displace the knee anteriorly and posteriorly. The peroneal nerve as paralyzed.

On April 9, 918, the stabilization operation as performed. At the same time the peroneal nerve as exposed at the point where it crosses the fibula, and considerable scar tissue as removed from this region. After the stitches as removed nonpadded cast as applied. Three weeks later the patient was supplied with brace.

In August, 920, the patient returned to work. He as re-examined on September 9, 920. At that time his knee as completely stable, and the function of the peroneal nerve had returned. The patient said that he had been working in logging camp.

CASE 4. J. C. male, aged 36 years, had twisted his right knee on August 3, 917, when he had fallen between two logs. He had been able to continue his work by not allowing his knee to extend completely. On March 4, 918, the internal semitendinous cartilage had been removed.

Examination of the right knee on August 5, 918, revealed that the anterior cruciate ligament as torn and that the external lateral ligament was also injured. In addition, there as some stretching of the posterior cruciate ligament. The knee could not be displaced backward to any great extent, yet the patient had genu recurvatum.

On September 20, 918, the operation for stabilization as performed. The nonpadded cast as applied after the stitches as removed and brace as supplied weeks later.

When this man as examined again on May 9, 919, as observed that the knee as stable as far as form and back and displacement were concerned, but that there as still some back knee. This caused slight disability.

I now believe that after operation on patients who present back knee, the knee should be placed in about 5 degrees of flexion for at least 6 weeks before movement is begun.

CASE 5. C. K. male aged 40 years, as examined on August 9, 919. It as found that the right leg could be displaced forward on the femur when the knee was in slight flexion. A diagnosis of torn anterior cruciate ligament as made. This man stated that he had dislocated his knee on March 5, 915, when he had jumped off a board. On August 28, 919, the stabilization operation as performed. The nonpadded cast as applied after the stitches had been removed, and six weeks later brace as supplied. A little over a year following this operation the patient returned to his work (logging timber). Letter written on June 9, 921, he stated that the operation as certainly successful success.

CASE 6. F. K. male, aged 24 years, seen on October 2, 918, because of an injury to his left knee which he had sustained while playing football. A diagnosis of torn anterior semitendinous cartilage and injury to the cruciate ligament of the left knee as made.

On May 17, 919, the left internal semitendinous cartilage as removed. And on October 9, 919, the stabilization operation as performed. Following this procedure the extremity as placed in nonpadded cast. Later the patient was given long knee cast.

This young man as re-examined on November 7, 920. At the time anterior displacement of the tibia on the femur as still present.

The displacement I believe, as probably due to relaxation of one of the fascial strips which occurred shortly after the operation. I have not been able to obtain permission to operate on this boy again. Meekison, however, reopened the incision on the medial side of the knee of one of his patients because of the same complication. One of the fascial bands, he found, had failed to hold and had to be reset in its position. The other was in place and had greatly hypertrophied.

Sufficient time has not yet elapsed to determine the outcome of the last 3 operations. One patient could not be traced.

SUMMARY AND CONCLUSIONS

The operation which has been described herein was first attempted because the patient had refused to have his knee opened, yet, because of the severity of his condition, required some stabilization procedure. From a cursory examination of the present technique, it would seem that fascial strips which are not drawn through bone cannot stabilize the knee joint. Practical application of this procedure over a long period of time has, nevertheless, except for 1 instance, been successful. This, it would seem, proves that it is not absolutely necessary to anchor fascial strips in bone in order to secure satisfactory stabilization. Moreover, Meekison, who had occasion to reopen the knee of one of his patients, observed that the fascial strip which had remained in place had greatly hypertrophied. This would indicate that fascial transplants applied in the manner just described have a normal physiological action.

While this stabilization operation has already been successfully carried out following severe in-

juries to the crucial and collateral ligaments, it is particularly applicable following minor injuries to these ligaments, that is, injuries which make wide exposure of the knee joint inexpedient.

Finally, as has already been stated, the stabilization operation now described is simple to perform; prolonged hospitalization is unnecessary, and the patient within a relatively short time is able to resume his former activities.

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bruising injury which could lead to interarticular changes and ultimate future disability. Further, the patella has a cosmetic value which must not be overlooked. Its removal obliterates the normal contour of the knee and creates an asymmetry between the injured and uninjured leg. There is generally, also, fear or apprehension expressed by the patient with respect to possible impairment of stability when removal is suggested. This is particularly true on the part of those engaged in occupations which require them to assume kneeling positions frequently, such as housewives, mechanics, plumbers, the clergy, and so forth. From the standpoint of a compensation or insurance case the removal of a whole bone, sesamoid or long bone, and the resultant defect, constitutes in itself substantial damage and potential disability.

3 *Plastic tendon repair and removal of loose fragments.* The limitations and disadvantages of the two preceding methods of dealing with the problem of fractures of the patella, from a physiological, anatomical and economic standpoint, have led to the growing popularity of a third school of thought which advocates the removal of all but a single attached fragment. This fragment may form either the distal or the proximal pole of the patella and the opposing patellar tendon is sutured to and through this remaining fragment.

To evaluate the appropriateness of this principle which I recommended years ago, many of the leading fracture surgeons were canvassed by questionnaire, with the result that 113 surgeons responded as having used this method on from 1 to 39 cases. A total of 554 cases have been studied. Of this number 479 have been analyzed with respect to age, sex, type of fracture, number of days between operation and beginning of weight-bearing, period of limited function, length of time between operation and return to work, and resulting ultimate partial permanent disability. There were 75 cases with incomplete statistical data but sufficient information was available from the many comments to prove valuable in making deductions. The 479 cases were divided into two groups. The first 424 cases comprised fractures operated upon within 2 weeks after injury. The second group, consisting of 55 cases, included those operated upon after the 2 week period.

In this series of cases the average age was 40 years. When one considers the ages by decades it is quite evident that this fracture seldom occurs in the very young and very old, and is distinctly a fracture of middle life. Males outnumbered females almost two to one.

Simple comminuted fractures were by far the commoner type in which this procedure was used, although it was used in a large group of simple fractures that were not comminuted. It is interesting to note that this method proved quite adaptable in 56 compound fractures.

Three hundred and fifty-five fractures were operated upon within 2 weeks. In 69 additional cases the exact day was not designated, but other circumstances reported seemed to indicate that they were operated upon early, so therefore they are considered in this group. The average number of days between accident and operation in this group was 3.6 days. However, there were 104, or 29 per cent, operated upon within the first 24 hours and 198, or 55 per cent, within 3 days, while 287, or 80 per cent, were operated upon within the first week and only 68, or 20 per cent, during the second week. Many of the fractures operated upon within a few hours were compound injuries in which débridement and clean up offered a chance of primary closure and healing. It was interesting to note that the more experience a surgeon had had with this technique the earlier he operated.

Of the 55 patients operated upon more than 2 weeks after injury, in 21 repair was done within 2 and 4 weeks, and 16 more were operated upon within 3 months. In this group are the fractures that were referred late to the surgeon, conservative treatment having failed to bring or hold the fragments together. There were 15 compound fractures which, due to tissue injury, infection, and other complicating circumstances, were unsuitable for early closure. Also there were 15 cases of nonunion or separation of fragments, following previous operations to approximate the fragments with wire and other suture material around and through the fragments. The necessity of a secondary operation probably contributed to a portion of the ultimate disability in 8 of these cases, 2, 5 per cent, 2, 10 per cent, 1, 15 per cent, 2, 20 per cent, 1, 30 per cent. Several of the patients in this group had complications of such importance that repair of the patella and tendon was necessarily delayed.

Not all of the reports gave the period of immobilization, but of the 316 cases in which this question was answered the average period was 4.17 weeks. Among these 16 had only a compression bandage after operation, and 67 had 2 weeks or less immobilization. The period of immobilization varied with the seriousness of the injury and complications. Some surgeons, using stainless steel wire and other nonabsorbent, or slowly absorbent, suture material, believed that immo-

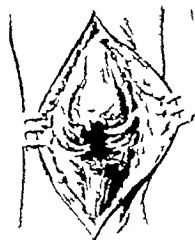


Fig. 2



Fig. 4



Fig. 3

Fig. 2. Fracture of lower portion of patella, with separation of fragments and shredding of tendon fibers between fragments. Longitudinal hemilinear incision. Skin flap reflected. Patellar region exposed.

Fig. 4. Small lower fragment removed. Shredded tendon fibers cut off. Edges of fractured patella smoothed.

Fig. 3. Drill holes identified as they pass through substance of patella, with kangaroo tendon suture in place. Flap of bronze catgut or stainless steel wire may be used.

Fig. 3. Lower patellar tendon drawn snugly against patellar fragment and kangaroo suture tied securely. Capsule and tendon structure closed.

bilization was not of major importance and that the suture and compression bandage were sufficient.

Severe complications and long bed confinement in 79 cases and conservative surgical judgment which kept patients off their feet in perhaps an equal number more raised the average time before walking was allowed to 5 weeks. Contrast this to the 75 who were allowed to walk within 2 weeks and the 76 within 3 weeks, and it will appear reasonable that without complications to interfere restricted flexion with early weight bearing prevents atrophy and gives confidence both of which are essential to a good result.

The average loss of time from work was 9.9 weeks for the 268 cases reported upon. Of this total number there were 189 fractures of the patella having no complications that had an average of 8.3 weeks loss of time. There were 79 cases with complications whose average loss of time from work was 4 weeks. There were students, clerks, teachers, and many others who were away from work only a short time. On the other hand, those engaged in more active occupations had a longer period of disability. Liability and compensation insurance as well as various types of psychoses, often entered into this picture. Further one must remember that 78 of these patients were between 50 and 60 years of age and

63 others were over 60 years of age. These fractures, when the patient is past middle age, require maximum healing and rehabilitation time.

In the consideration of the subject of disability of any impaired part of the body there is such a tremendous personal equation that must be taken into account, in connection with every opinion, that one must be guarded in the estimation of percentages. There may be a slight quadriceps weakness which in one individual is of no consequence while for another it would constitute considerable disability. Likewise, one might have extensive loss of normal flexion and have relatively little disability for almost any type of labor.

Four hundred and thirty three reported disability aspect of disability 350 were reported with disability leaving 83 cases with partial disabilities. Of these 83 cases 73 had disabilities under 5 per cent which left only 10 cases with disabilities above 5 per cent. Among the 10 cases with disabilities there were 61 who had complicating injuries, disease, or infection that contributed to the estimation of their partial permanent disability. Of a total series of 433 cases this included only 1 patient with fractures of the patella without complications who had disabilities of up to 5 per cent in severe cases, the results were spoken of as excellent.

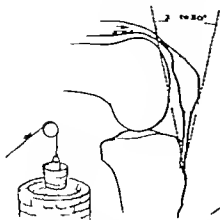


Fig 4



Fig 5

Figs 4 and 5. The patella by carrying the quadriceps tendon away from the femoral condyles lessens the leverage action of that muscle and lessens the effort required for extension. The removal of the patella decreases this leverage action—by an angle of 25 to 30 degrees—and greater effort is required to extend the leg. The principle of the patella action is similar to the levered effort exerted when a bucket of water is drawn up over a pulley rather than when it is dragged over the edges of the well.



Fig 6



Fig 7



Fig 8

Figs 6, 7 and 8. Types of fracture of the patella in which removal of all but one fragment and plastic repair of the tendon is particularly indicated.

Fig 6. The small single fragment should be removed.

Fig 7. The comminuted fragments should be removed.

Fig 8. The lower fragment of transverse fracture should be removed.

ended, and satisfactory. From a compensation standpoint most fractures of the patella, even a disability that must be considered in making a settlement, while a year or the impairment of function will be negligible. It is interesting to note that in this series there were 56 compound fractures of the patella and out of these (26) had disabilities. Of the cases 10 had complicating injuries, which left uncomplicated compound fractures of the patella with disability. Fifteen of the 26 patients had a disability between 5 and 15 per cent and

8 had more than 15 per cent disability. In addition to these there were 3 compound fractures with admitted disability in which percentage was unestimated. This left 30 compound fractures of the patella with no disability.

Among the conditions incident to this operation that contributed to disabilities were several to which I wish to direct some attention.

First, post-operative infections. There were 4 of these and no explanation or reason was given for them. Three were serious and long disabling with 50, 70 and 15 per cent disabilities. The

have been several valuable suggestions and modifications for this procedure. All of them aim toward accomplishing and restoring better and more secure apposition of the opposing tendon ends. Hoyt and O'Donoghue suggested wire as a suture through, or around, the bone fragment and the opposing tendon. We have not yet tried stainless steel wire, but the many interesting and satisfactory results from its use would lead me to feel that there was considerable virtue in its security. As yet in none of these cases, in many of which patients were operated upon over 2 years ago, has it been necessary to remove the wire. Therefore, the wire apparently did not cause irritation with functional activity. Contraction of the quadriceps has led occasionally to difficulty in reapposition of the fragment and tendon. The low tourniquet often contributes to this. We have found that a traction suture through the patella helped in bringing the tissues together. However, Stern states that inadequate relaxation is accomplished by the use of either a spinal anesthesia or an extensive infiltration with one-half of one per cent novocain directly into the bellies of the quadriceps muscles, which makes it much easier to oppose the fragment and the tendon.

Prince, in his April, 1940, letter to the Orthopedic Correspondence Club, modified the technique not only by suture of the tendon to the fragment, but also by embedding the upper end of the tendon under the periosteum of the upper portion of the fragment. Stern has modified this still further. He also bores holes from above obliquely downward in the patellar fragment, so that they come out on the fractured surface just in front of the articulating portion. The suture material is introduced into the patellar tendon about an inch below the upper end, and then the tendon is brought into contact with the patellar fragment from the lower border across the fractured base and up over the top of the patella. Here, after the method of Prince, the upper end of the tendon is embedded under the periosteum of the patellar fragment.

These modifications may add to the better union and healing of the repaired patellar tendon and have the virtue of bringing the remaining patellar substance down farther on the condyles which is so essential to the strength of the quadriceps action. A factor of technique which we believe of extreme importance to the restoration of good function is the plastic repair of the capsule and ligamentous substance which is usually torn on either side of the patella.

Among those who submitted cases were 11 surgeons who reported 10 to 39 cases, inclusive, and 24 surgeons who reported 5 to 10 cases inclusive, or a total of 35 surgeons with considerable experience with this procedure. The largest groups reported were Boyd, 39 cases, Hoyt, 24 cases, and Dillehunt et al., 19 cases, each with generally rather gratifying results.

CONCLUSIONS

Bear in mind that this is not a comparative evaluation of the various approaches to the treatment of fractures of the patella, but rather a study of a large group of cases in which a single operative principle has been applied. The conclusions are not my own but are the expression of the averages, clinical data, and opinions of those who furnished the cases. However, they verify convictions held ever since I recommended this procedure.

1. Fracture of the patella is common in middle life and seldom occurs among the young as in females.
2. It occurs in males more than twice as often as in females.
3. Communited fractures are twice as frequent as any other.
4. Compound fractures deserve the same consideration here as such fractures elsewhere.
5. The more familiar the operator becomes with this technique the earlier the fracture comes to surgical repair.
6. If there is extensive damage to integument and underlying tissues many prefer to delay operation (average 3.5 days) and allow a "tissue comeback."
7. This fracture is often associated with other complicating injuries that influence the ultimate outcome.
8. Early weight-bearing with restricted flexion should be encouraged (1½ to 3 weeks), provided complications do not interfere.
9. Loss of time away from work is directly proportionate to the severity of the injury and complications, 8 weeks for uncomplicated fractures and 14 weeks for complicated fractures.
10. There were but 22 fractures that were not complicated by other injuries that had disability completely studied. In none of these was the disability over 15 per cent. The average was 7.5 per cent while those with complications had an average of about 16.5 per cent of function.
11. This large esamoid has an important functional value to the knee joint particularly when fully flexed (figs 4 and 5), in that it elevates the

indicates with fine precision that the normal tissues are unable to tolerate the intensity of the radiation that is being administered. Appearance of this sign is an indication for immediate reduction of the intensity of treatment or of the size of the field.

Injury to Blood. The intracavitary application of radium is not complicated by any noteworthy injury to the blood elements and with rare exceptions the same holds true for external radiation. Lavedan and others have proved that treatment with the most intense methods of external radiation with radium as well as x-rays results only to a slight and temporary leucopenia followed by restoration to normal within a short period after the completion of treatment.

In the writer's experience the white blood cells of a small proportion of patients have a special sensitivity to radiation. I estimate the incidence as less than 5 per cent. In these cases the first few exposures result in an unusual diminution of the leucocytes, sometimes necessitating an interruption of treatment. With these rare exceptions, no serious or permanent damage to the blood-forming organs is encountered following the fractional method of radiation.

Wintz admits that under certain conditions with the massive dose treatment severe blood changes finally leading to death cannot be totally avoided, but he believes that this risk must be taken in dealing with a lethal disease. In view of the favorable results of the fractional method of treatment, this risk does not seem justified.

The general apprehension regarding the dangers of injury to the blood-forming organs accompanying massive radiation for cancer of the cervix is not supported by the most authentic evidence. All difficulties can be eliminated by a voiding the single massive radiation and by identifying the occasional patient with hypersensitivity of the white blood cells.

Injury to Bladder. Injury to the bladder as a result of radiation in cervical cancer is uncommon if the treatment is given with reasonable precision. Serious damage to the bladder can occur only as a result of faulty radiation. A mild irritation of the bladder mucosa may become evident during treatment; the symptoms, however, generally disappear within a short period. Small superficial erosions of the bladder in case are sometimes observed on cystoscopic examination soon after intracavitary radiation. These lesions are said to be more common than has been generally supposed. They apparently heal within a short time and probably result in no serious permanent damage. On the whole bladder in-

jury does not constitute a serious problem in the radiotherapy of cervical cancer.

Injury to Rectum. The rectal mucous membrane is certainly one of the most, if not the most, sensitive tissues in the body to radiation. This fact, combined with the proximity of the rectum to the radium foci placed against the cervical lesion exposes the rectum to possible radiation injuries. Before the dangers associated with the uses of radium were adequately recognized, serious rectal damage often resulting in rectovaginal fistula was not uncommon. Today this complication is extremely rare. It must be noted that advanced stages of the disease untreated result in rectovaginal fistula in a small but definite proportion of cases, so that the presence of this condition does not necessarily indicate an incorrect radiation.

Radiation effects upon the rectal mucous membrane result in definite clinical signs which vary in degree in proportion to the intensity of the radiation. The first and mildest reaction consists of a watery diarrhea without abdominal pain, with two to four liquid stools daily. These signs develop frequently during the beginning of the third week of external radiation when a little less than half of the treatment has been completed (4000 r units or 50,000 mg hrs.). This reaction naturally develops somewhat earlier in some patients. It constitutes a highly important clinical sign in that it indicates that the level of tolerance has been reached. A reaction of this degree does not require any changes in the radiation with the exception of reducing the size of the skin portal. The importance of making this one change can hardly be overemphasized.

If the rectal reaction becomes more severe, resulting in six to eight stools daily accompanied by colic-like pain, the indication is that the radiation is too intense. Under these circumstances either the daily dose must be reduced or the size of the field diminished or the treatment must be discontinued for several days or longer.

A profuse, severe diarrhea accompanied by colic-like pain is due to overdosage and should be avoided. Healy has directed attention to severe intestinal reactions occurring toward the end of the radiation and simulating the clinical picture of acute appendicitis.

Late postirradiation sclerosis of pelvic tissues. Late sclerosis of the pelvic tissues may occur years after intensive radiation for cancer of the cervix. This state may be accompanied by occlusion of the vagina and cervix followed by proctometragmal sclerosis, rectal obstruction, and occlusion of the ureters followed by pyelonephro-

sis or pyelonephritis Regaud and Hermet have made a study of this late complication They have described them as tumor formations usually located in one side of the pelvis and frequently involving the rectum, uterus, and bladder In the beginning they are comparatively soft and lack the induration of a true recurrence The contour is diffuse and the mass is painful to the touch In one group of cases a closed pyometra with peruterine edema and diffuse parametrial inflammation simulates a local recurrence

The diagnosis of these lesions may be exceedingly difficult Such lesions may persist for many years before they disappear A pyometra can be excluded by careful exploration of the cervical canal In the other forms a differential diagnosis between postradiation sclerosis and recurrence is finally established only by the course of the disease

I have encountered several cases in which mild palliative radiation was given for suspected late parametrial recurrences The patients were discharged with an apparently hopeless prognosis Several years later information has reached me that these patients are alive and well There can be little doubt that these are examples of pelvic sclerosis and not recurrent carcinoma The importance of recognizing this possibility is obvious and one should avoid giving a hopeless prognosis in the face of this possibility

Postradiation intestinal obstruction resulting from benign stricture of intestine This complication, although rare, is of the greatest importance The writer has encountered two examples Jones of Cleveland has reported 7 cases Unless this possibility is considered, a diagnosis of recurrence is usually made The clinical picture is classically that of intestinal obstruction Jones has made the following observations

"In 520 patients having cervical carcinoma who received radiation therapy there have been seven known cases of benign stricture of the intestine caused by obstruction which might easily have been construed as, or confused with, metastatic deposits In five the obstruction was in a movable segment of the sigmoid and in two in the small intestine Since similar methods of therapy are in general use, it seems probable that the incidence of the lesion is greater than is surmised, and if similar cases have been attributed to metastasis in the past, the mortality statistics relating to metastasis from cervical carcinoma are open to question The intestinal obstruction developed in the seven patients from eight months to eight years after radiation therapy for cervical carcinoma If the condition actually is a benign stricture caused by irradiation, it is obvious that additional roentgen treatment would only aggravate the condition and hasten the end Therefore, a patient in whom unusual abdominal symptoms are present, particularly if they simulate intestinal obstruction, may have a stricture of the intestine and may be restored to normal health by resection of the colon

"Before attributing this disability to metastasis, thorough re-examination by sigmoidoscopic and roentgenographic studies should be made to eliminate the possibility of this curable complication Strictures in the small intestine are difficult to visualize unless the obstruction is practically complete Barium in large amounts is inadvisable, and therefore, exploratory operation is warranted, especially in patients in whom there is no evidence of recurring carcinoma in the pelvis"

Localized infection Before the more serious and sometimes fatal generalized infections are discussed, brief reference will be made to the less serious infections which remain localized and from which the patient generally recovers These may be divided into three groups

1 *Early pyometra* due to occlusion of the cervical canal and appearing toward the end or within several weeks after radiation This complication should always be considered and recognized as early as possible Dilatation of the cervical canal and drainage frequently terminates this complication

2 *Late pyometra* occurs from one to several years after treatment The condition has to be differentiated from recurrence The treatment is the same as for early pyometra Occurring long after treatment, the diagnosis is more likely to be missed

3 *Late infectious parametritis* This complication arises usually one to three years after radiation treatment It may be due to a reactivation of an old latent infection or to a new infection which becomes localized in tissues of a lowered resistance This inflammatory complication must be differentiated from recurrent cancerous disease

Localized and generalized infection during irradiation of cervical cancer Infection during the process of irradiation is by far the most important complication associated with the radiotherapy of cancer of the cervix, the 2 per cent mortality charged against this procedure being due almost exclusively to the activation of hemolytic streptococci by the radiation What are the circumstances under which this serious event occurs and how can it be avoided?

The incidence of hemolytic streptococci in cervical cancer is variously reported by different authors Dehler reports that most cancers of the cervix contain streptococci and that over two-thirds of these are hemolytic Clauberg, however, found nonhemolytic streptococci in 97 of 122 cases of streptococcal infection in cervical cancer Philipp considers that hemolytic streptococci are the most commonly encountered organisms as well as the most virulent, although not all hemolytic streptococci are virulent

In an effort to determine the virulence of the micro organisms, Ruge devised a clinical test which has been amplified by Philipp The Ruge-Philipp test determines the ability of the patient's micro organisms to grow in a medium containing the patient's own blood If the bac-

teria grow and multiply they are considered virulent. If they fail to grow or if they diminish in number they are considered of uncertain virulence. With this classification it was found that radiation treatment in the presence of a virulent streptococci resulted in 2 deaths (2 per cent). One patient developed severe complications and 48 had a smooth convalescence. Of 22 carriers of virulent streptococci 5 or 19 per cent died. 8 showed severe complications and 13 showed a smooth convalescence.

Many procedures have been advocated to combat this complication. Antiseptic douches, hypertonic salt solutions, copper salts, vaccines autovaccination, and antistreptococcus serum have been recommended. A chemical known as rubral has been tried in the Curie Institute. None of these procedures have succeeded in effectively eliminating this complication.

Baclenue reports that among 44 cases of advanced carcinoma of the cervix treated intensively between 1912 and 1927 by external radiation 7 or 16 per cent died during treatment of infectious complications whereas between the years 1928 and 1930 only 1 of 19 patients died of infection, 5 per cent. This author is probably correct in attributing the difference to an improvement in the technique and distribution of the radiation. It would seem from this evidence and other data that cautious, well distributed radiation diminishes the danger of infectious complications.

Since the introduction of sulphanilamide and its derivatives, several reports have appeared in the literature indicating their value in the treatment of these infections. In 1938 Goff reported a striking result in a pelvic cellulitis complicating radium treatment of a carcinoma of the cervix. He used sulphanilamide. In 1939 Bowring and Fricke reported the cases of 3 patients treated by sulphanilamide with excellent result.

SUMMARY

Most of the complications associated with the radiation treatment of cervical cancer are due to a faulty technique and are avoidable.

Edema of the skin and irritation of the rectal mucosa are two important signs indicating that the limits of tolerance have been reached. These signs, particularly the latter should be

carefully looked for and used as guides in the intensity of treatment. Careful attention to these signs at once obviates most of the avoidable complications.

3. Postirradiation pyometra and sclerosis of the pelvic tissues occurring one to several years after treatment may simulate recurrent cancer so closely that a differential diagnosis is impossible. This source of error should be considered in rendering a prognosis and planning treatment in this group of cases.

4. Signs of intestinal obstruction appearing months or years after irradiation of cervical cancer should raise the suspicion of benign stricture of the intestine.

5. Infection constitutes a notable exception. This complication is largely unavoidable. The activation of latent hemolytic streptococci is a real danger and is associated with 1 to 2 per cent mortality. Virulent hemolytic streptococci are probably less frequent in early lesions.

6. A bacteriological examination should be made in every case before treatment as the infected cases require special attention.

7. An effort should be made to combat the infection by the best methods of anti-streptococcal therapy. Sulphanilamide has been used with considerable success.

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THE SIGNIFICANCE OF THE VENOUS CIRCULATION ABOUT THE ELBOW IN THE PATHOMECHANICS OF VOLKMANN'S CONTRACTURE

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THE concept that venous obstruction plays an important rôle in the mechanogenesis of Volkmann's contracture of the upper extremity has been premised, in great part, on the belief that the venous communication between the deep and superficial venous systems in the elbow region is a single venous channel and is susceptible to compression, as by a subfascial hematoma, within the confines of the antecubital compartment. The anatomical facts to be related in this investigation indicate that the venous communications between the deep and superficial networks are numerous and that the collateral system is widespread and well protected. This adds further evidence that the concept of venous obstruction as an important factor in the causation of Volkmann's deformity is untenable.

ANATOMICAL CONSIDERATIONS

The venous patterns about the elbow region, in the lower arm and in the upper forearm, were recorded by the writer from a study of 67 upper extremities—34 left and 33 right—in 34 human male cadavers, of which 19 were colored and 15 were white, and with ages varying from 22 to 85 years with an average age of 57 years. Anatomical dissections of the venous network in the upper extremities of 10 additional adult human male cadavers were made by the writer, following roentgenographic studies of the venous circulation with a radiopaque medium—30 per cent aqueous solution of sodium iodide.

The patterns of the superficial veins of the upper extremity have been investigated extensively and reported by Berry and Newton, Okamoto, and Charles. The observations in the present study were confined to the deep venous systems and their communications. In the hand and forearm the fetal type persists throughout life and the superficial veins are dominant, in the arm and axilla the deep veins are most important. With

rare exceptions the deep arm and hand in each case are the ulnar arteries, and each artery is accompanied by two veins.

Brachial veins. The brachial veins are commonly two in number, the ulnar being larger than the radial. They join to form the axillary vein at the level of the lower border of the subscapularis muscle. In some cases the axillary vein appeared to be formed by the union of the brachial veins, usually the ulnar, and in others, it appeared to be a single vein. In the same cadaver was eight times more of the symmetry of their arrangement. In some cases, the brachial veins were replaced by a single vein. Occasionally, the ulnar vein was developed, the basilic receiving the venous return of the arm. It was frequently the medial or ulnar vein (accompanying the inferior ulnar artery) was very well developed and appeared to terminate instead of one of the brachial veins, the ulnar does. In one specimen both brachial veins were tied into the deep brachial vein. In another, the ulnar vein terminated in a large medial collateral vein. The more common arrangement is illustrated in Figures 2 to 8.

Radial and ulnar veins. The radial and ulnar veins, the ulnar being usually the larger, joined within the antecubital fossa to form the brachial veins. The ulnar veins receive the venous return of the posterior interosseous veins deep to the pronator

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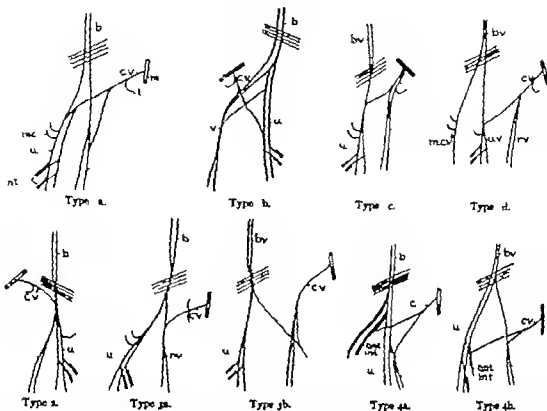


Fig. Diagrammatic representations of variations in the formation of the communicating vein of the elbow in 67 upper extremities of 34 bronze cadavers. The incidence is as follows: type 1a occurred in 16 cadavers bilaterally and in 28 cadavers unilaterally; types b, c, d and e, each in each or unilaterally type 3a, in 3 cadavers unilaterally; type 3b, in each or unilaterally type 4a, in each or unilaterally and in each or bilaterally and type 4b,

in each or bilaterally; b, brachial vein; r, radial vein; u, ulnar vein; mc, interosseous vein (anterior and posterior); c, communicating vein of elbow; cephalic vein = c, median cubital vein = mc, lateral cubital branches, m, medial cubital branches, m, medial cubital vein. The obliquely parallel lines represent the relative position and course of the fibers of the lacertus fibrosus.

teres and flexor digitorum sublimis muscles and medial to the bicipital tendon. The venous patterns at this juncture varied considerably (Figs. 1 to 8).

High formation of the radial and ulnar arteries from the brachial artery in the upper or middle thirds of the arm was present bilaterally in 3 and unilaterally in 5 cadavers, while in one specimen the radial and ulnar arteries arose directly by division of the axillary artery. In these instances the radial and ulnar veins ascended in the arm and either terminated separately in the basilic vein or joined just prior to doing so (Fig. 3). In one specimen in which there was a high division of the brachial artery the radial veins terminated in the cephalic vein, while the ulnar veins ascended in the arm to end in the basilic vein (Fig. 1 Type 3b).

COLLATERAL VEIN SYSTEMS ABOUT THE ELBOW REGION

1. *Communicating vein of the elbow* (Figs. 1 to 8). The communicating vein of the elbow was always anastomotic but the valves of the deep and superficial veins were so placed as to require the blood to flow from the depth to the surface. It terminated in the cephalic vein, above or below the origin of the median cubital vein, or in the median cubital vein, close to the origin of the latter from the cephalic vein, or occasionally, into both veins. In Figure 1 the formation of the communicating vein has been grouped broadly into four types. In the first type, the most frequent, this vein received branches from the radial and ulnar veins. In the second type the communicating vein arose from the venous plexus formed by the juncture of the radial and ulnar

veins, in the third type this vein received a communication only from the radial veins, and in the fourth type it was formed by branches from the anterior interosseous and radial veins. In all types the communicating vein received additional branches from the veins draining the lateral condylar muscles. Symmetry of the venous pattern in this region on both sides of the same cadaver was slightly more frequent than asymmetry.

In this investigation there were observed 3 distinct avascular collateral veins or venous networks in the elbow region, in addition to the so called communicating vein (Figs 2 to 8). That there are in addition to these 4 communications, other collateral systems present about the elbow region, which are too delicate to delineate from gross dissections, is evidenced by the complex networks visualized by means of a radiopaque medium (Figs 7a and 8a).

2 A large communication was almost invariably present between the ulnar veins and one of the brachial veins or the basilic vein, by way of the medial collateral vein that lay ventral to the trochlea and brachialis anticus muscle and deep to the flexor group of muscles arising from the medial humeral condyle (Figs 2, 3, 4, 6, 7, and 8).

3 A less constant communication arose from one of the lateral condylar veins, which pierced the triceps muscle substance and coursed posteriorly along with the radial nerve in the radial sulcus, joining the deep brachial veins (Figs 2, 3, 5, 7, and 8).

4 A communication, the least frequent of all, arose from the ulnar or medial collateral veins, passed behind the internal condyle of the humerus in relation with the ulnar nerve, meeting the veins which accompanied the superior ulnar collateral artery, and terminating in the basilic vein (Figs 7 and 8).

ROENTGENOGRAPHIC STUDIES WITH RADIOPAQUE MEDIUM

How effectual these collateral systems may be in transferring blood from below to above the elbow region was illustrated by roentgenography following the injection of a radiopaque solution (30 per cent sodium iodide) into the upper extremities of 10 cadavers.

In some of the specimens the brachial veins alone were ligated just above the elbow region. The solution of sodium iodide was injected into one of the radial or ulnar veins, and it appeared immediately in the arm above the site of ligation (Fig 2). In these instances all of the communicating systems about the elbow region were intact.

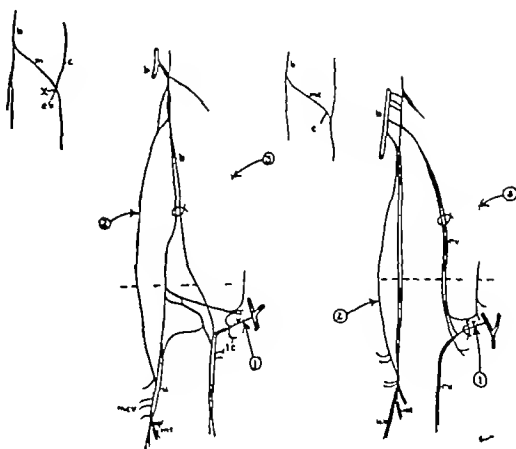


Fig 2

Fig 3

Fig 2 Scheme of (a) the superficial and (b) the deep veins and communicating systems 1, 2, and 3 (see text) of the elbow region. In this specimen the brachial veins were ligated above the elbow region but this did not interrupt the proximal flow of a radiopaque medium in the arm. *b v*, brachial veins, *r v*, radial veins, *u v*, ulnar veins, *int v*, interosseous veins (anterior and posterior), *b*, basilic vein, *c*, cephalic vein, *m c*, median cubital vein, *c v*, communicating vein of the elbow (*v*). The interrupted horizontal line represents the level of the elbow joint.

Fig 3 Scheme of (a) the superficial and (b) the deep veins and communicating systems of the elbow region in a specimen with high division of the brachial artery in the upper third of the arm. Ligatures about the radial veins (which lay superficial to the ulnar veins) and the communicating vein of the elbow failed to interrupt the proximal flow of a radiopaque medium in the arm. *b v*, brachial veins, *r v*, radial veins, *u v*, ulnar veins, *int v*, interosseous veins (anterior and posterior), *b*, basilic vein, *c*, cephalic vein, *m c*, median cubital vein, *c v*, communicating vein of the elbow (*v*). The interrupted horizontal line represents the level of the elbow joint.

In 10 specimens the communicating vein of the elbow was ligated just distal to its termination in the cephalic or median cubital veins, and the brachial veins were ligated just above the site of their formation, through very small incisions. The contrast medium was injected via one of the ulnar or radial veins, which was ligated just distal to the cannula, and the specimen was roentgenographed during the injection. The solution, despite these ligations, immediately entered and coursed up the arm in every instance, as noted in the roentgenograms (Figs 4a, 5a, 6a, 7a and 8a), and by the immediate escape of the fluid (colored for purposes of recognition) from the cut surface of the proximal end of the specimen.

EVALUATION

It is generally accepted that external constriction is not essential for the development of Volk-

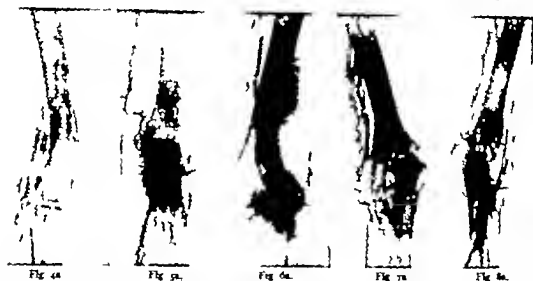
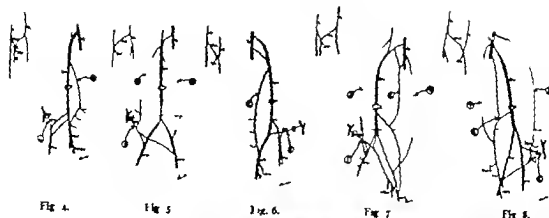


Fig. 4. This figure (as Figures 5, 6, 7 and 8) is a schematic representation of (a) the superficial arteries and (b) the deep arteries and communicating systems of the elbow region of cadaver specimen. The brachial artery is ligated above the elbow joint and the communicating veins of the elbow are heated just prior to its entrance into the superficial system at point A. The failure of these ligatures to interfere with the proximal

flow of radiopaque fluid in the arm is illustrated in the corresponding Figure 4a. (Figures 5a, 6a, 7a and 8a correspond to Figures 5, 6, 7 and 8) a brachial artery, radial artery, ulnar artery, and interosseous artery (anterior and posterior), b basilic artery, cephalic artery, c median cubital artery, communicating artery of the elbow (A). The interrupted horizontal line represents the level of the elbow joint.

maintains contracture and that a fracture need not be present (Hill and Brooks). Although peripheral nerve lesions may complicate the clinical picture they are not constant and are not as a rule anatomically defined.

The protagonists of the concept of venous obstruction as an important factor in the etiology of Volkmann's contracture, emphasize the experimental evidence of Brooks (2), Middleton (3) and Wertheimer, Dechaine and Fried, who produced a condition resembling ischemic contracture

of muscle by sudden venous occlusion. They suggest that the fundamental pathomechanics of this condition are abnormal pressure conditions—by a subclavicular herniation—in a limited space—the antecubital compartment—containing muscles and surrounded by resistant fascia and bone and drawn by powerful anatomical forces that factors obstructs. Middleton (3, 4) has discussed this anatomical arrangement in the elbow region; he suggests that a venous plexus with a diameter of about 2 centimeters drains the deep

structures of the entire forearm. This concept is supported by descriptions of the venous network of the elbow region in most anatomical textbooks and has been accepted as factual by many writers on the subject of Volkmann's contracture (Jones and Lovett, 14, Meehan, Garber)

There is increasing evidence, however, that arterial obstruction rather than venous obstruction plays a significant rôle in the etiology of this deformity.

1 Contractures of limbs in experimental animals were observed to occur following the production of arterial obstructive lesions, by Von Nario, Brooks, Johnson and Kirtley, 3, Wilson, and Griffiths, 10. It was noted by Jepson, and by Burman and Sutro that venous stasis alone was insufficient to produce permanent contractures of the limbs, and that, in addition, proximal constriction of the soft tissues was necessary.

2 Exploration in cases involving the upper extremity in the acute or threatening stage failed to reveal evidence of subfascial hematoma in the antecubital fossa. The muscle bellies were found to be engorged and discolored, but this was more common in the brachialis anticus muscle than in the forearm flexor muscles. There were subcutaneous extravasations and small hematoma-formation about the fracture site but no occlusion of the main veins could be demonstrated. In almost all of the arms explored, there were lesions affecting the brachial artery—vasospasm, incarceration between bony fragments, angulation, laceration or tear. In some arms in which the injured portion of the brachial artery was resected, there was evidence of injury to the adventitia or media or to both of these layers of the resected arterial segment (Griffiths, 10, Jones, 13, Plewes).

3 Volkmann's contracture has followed proved instances of arterial occlusion. Griffiths (9, 10) noted that in 3 cases in a series of 20, patients operated upon for arterial embolism, developed typical Volkmann's contracture—one of the forearm and hand, and two of the calf and foot—despite successful restoration of the arterial circulation. Similar contractures following arterial obstruction in the lower extremity have been reported by Grieg and by Dieulafoy.

4 The evidence derived from the anatomical material in this investigation, that a sufficient

collateral venous circulation exists normally in the elbow region, well protected between muscle planes and external to the confines of the antecubital fossa, indicates that the theory of Middleton, on which the protagonists of the concept of venous obstruction have relied to a considerable extent, is untenable.

CONCLUSIONS

The belief that arterial obstruction plays a more significant rôle than venous obstruction in the pathogenesis of Volkmann's contracture is receiving increasing clinical and experimental support. To this is added evidence that the theory of Middleton, on which the protagonists of the concept of venous obstruction have relied, is untenable. The anatomical studies in this investigation indicate that a widespread venous anastomosis exists normally in the elbow region, well protected between muscle planes and external to the confines of the antecubital space.

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REINFORCEMENT OF THE DELTOID LIGAMENT FOR PRONATED FLAT FOOT

Inversion Fasciodesis of Os Calcis

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SOLUTION of the problem of flat foot has been sought by many in both surgical and nonsurgical procedures. The latter based mainly on the belief that acquired flat foot is a consequence of muscle inadequacy has led to the elaboration of a system of therapy which depends on foot braces, shoe modifications and a ritual of muscle exercises. In our experience even when religiously prosecuted, these have proved futile in the cure of the truly pronated flat foot. In the main, the failures have been attributed to lack of co-operation, but the fact that pronation may occur even in the presence of a well developed musculature seems to have been overlooked. Despite this, and possibly in deference to the natural reluctance of parents to submit their children to surgery for relief of what appears, at outset, to be a relatively innocuous affliction, the conservative treatment has been maintained and by some extolled.

That the affliction is not so innocuous, nor the conservative treatment so effectual is indicated by the variety of surgical procedures which have been devised from time to time. Moreover the very multiplicity of the suggestions is, in itself proof that no single method of surgery has thus far adequately solved the problem. Practically almost every important bone, muscle, ligament, and joint of the tarsus has been surgically attacked. Generally speaking the procedure employed fall into two categories—the anterior operations directed toward correction of the depressed longitudinal arch and the posterior directed toward inversion of the pronated heel.

That one or another of the anterior group of operations may successfully correct a true planus need not be denied. But whether the correction of the anterior deformity can effect a correction of the posterior deformity by pressure from below may be seriously doubted. It is, in fact to the failure of such efforts that various procedures intended to supinate or invert the everted hind foot owe their origin. On the whole the anterior group of operations has proved to be more successful in restoring the longitudinal arch than the posterior

group has been in overcoming the pronation of the heel. In retrospect, it appears that these results might have been expected because of the failure to correct the pronation deformity at the apex of its angle of deviation—the subtalar joint. The realization of the importance of the proper handling of this joint above that of any of the other tarsal joints in the treatment of pronated feet seems to be the very basis of the good results obtained by Clark and later by Zidek.

In part, some of the difficulty which has been encountered is due to the fact that two anatomically different situations have been grouped together as a single clinical entity. Anatomically the foot is a unit composed of a number of separate segments. Physiologically the foot consists of two separate organs, the hind foot and the fore foot. *Pes planus* describes a flattening of the longitudinal arch, that is, a change in anatomical relationship between fore foot and hind foot, and *pes valgus* a rotation of the hind foot in relation to the longitudinal axis of the superimposed leg. *Pes plano-valgus* describes the combined form.

Obviously the cure of *pes planus* must be by surgical means which act across the mediotalar joints to stabilize the fore foot in relation to the hind foot while the cure of *pes valgus* must be effected across the subtalar joint so as to stabilize the hind foot in relation to the leg. In the absence of a stabilized hind foot, it is useless to discuss the problem of the longitudinal arch.

By comparison with the lower or anthropoid forms, in which the arch is depressed and the os calcis everted, the human hind foot is separated. Naturally the development of the longitudinal arch has been associated with this inversion of the heel, and with *supination* has been considered the mechanism of its accomplishment.

Largely under the influence of Keith, who expressed the opinion that "with the maintenance of the normal arch, ligaments are not directly concerned" but that "the longitudinal arch of the foot is dependent on properly and automatically balanced muscles in leg and foot," the belief has been propagated that the cause of flat foot is a muscle weakness. Even Morton, who stated

categorically that "the term 'balance' as applied to foot structure does not refer to muscle activity but to the arrangement of the bones and ligaments which furnish a stable base upon which body weight can be supported with the least demand for muscular exertion and propelled evenly balanced upon the lever axis," admitted the importance of the flexors of the foot in elevation of the arch and in rotation of the os calcis. Though he denied the significance of the supinating mechanism, Morton concluded that the longitudinal arch appeared in consequence of the leverage action in a foot in which the body weight had shifted from the outer toward the inner side of the foot. As a consequence of such teaching, the nonsurgical treatment has been designed to increase the power of existing invertors, while the surgical treatment has been devised to supplement their action either by fusion or by actual muscle transplantation.

More recent observations upon the embryology of the human foot cast interesting light upon the etiology of flat foot. Boehm showed that at about the end of the third intrauterine month, the foot is held in a position of marked supination, adduction, and internal rotation, i.e., in the position of extreme equino cavo-varus. Thereafter the supination tends to recede and though still present at birth, the appearance of the adult foot is acquired slowly and as a result of *pronation*. This general impression was confirmed by Boeker in his study of the prints of infantile feet. At birth, the foot is held in supination and the sole of the foot, as well as the big toe, preserves many of the characteristics of the prehensile foot. When the infant begins to walk, but little weight is carried by the big toe which is still prehensile and is not used for progression. The thrust is balanced on the outer side and the fore foot acts as the steadying force while the heel is raised from the ground. At the age of 2½ years, most of the weight is still over outer side of foot and the longitudinal arch appears flat. By the age of 10 the body weight has moved toward the inner side, the big toe gives evidence of greater weight bearing, and the longitudinal arch is fairly well formed. By 14 years, with increasing weight and medial shift of the thrust, the big toe transmits a larger proportion of the body weight and a still higher adult type of arch is present.

In fact, it appears that active pronation is the fundamental process and that the development of the longitudinal arch is the result of the conversion of the fully supinated foot into one characterized by relative pronation of the fore foot. In any flexible foot it can readily be demonstrated that with the heel fixed, relative pronation of the fore foot invariably results in an increase in the

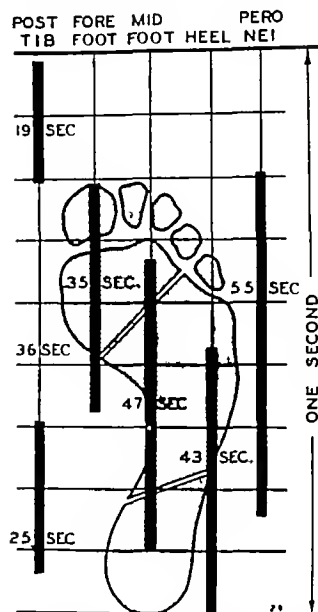


Fig. 1. Average sequence and duration of weight bearing on heel, midfoot, and forefoot as related to sequence and duration of contraction of the posterior tibial and peroneal muscles (From Schwartz, loc cit)

height of the longitudinal arch. Indeed, it was in the hope of accomplishing exactly this effect that the "skew" elevation of inner border of heel and outer border of the sole of the shoe was devised.

It is in the realization of the importance of the fore foot pronating mechanism that the studies by Schwartz acquire added biological significance.

"The heel receives and supports body weight for 0.436 seconds. The posterior tibial muscle contracts simultaneously with placement of the heel on the floor, but its duration of contraction is only 36.1 per cent of the total stance phase of the step, 0.694 seconds, 57.5 per cent of the total time the heel is on the floor. Therefore it is evident that this short period of reflex function of the tibialis posterior does not prevent the foot from pronating while walking.

"This too early discontinuance of a positive force that could prevent pronation is accompanied by peroneal contraction which further provokes the characteristics of pronation in each step. The peronei begin to contract 0.166 seconds after the heel contacts the floor and continue to contract for 79.8 per cent of the stance phase of the step, as against 36.1 per cent previously stated for the posterior tibial" (Fig. 1).

Here again the relative importance of the pronating mechanism of the fore foot as contrasted with the supinating mechanism of the hind foot is demonstrated. Contrary to the general belief, it is the absence of active fore foot pronation rather than of active hind foot supination that leads to pes planus. Without a powerful pronat-

REINFORCEMENT OF THE DELTOID LIGAMENT FOR PRONATED FLAT FOOT

Inversion Fasciodesis of Os Calcis

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SOLUTION of the problem of flat foot has been sought by many in both surgical and nonsurgical procedures. The latter based mainly on the belief that aquired flat foot is a consequence of muscle inadequacy have led to the elaboration of a system of therapy which depends on foot braces, shoe modifications, and a ritual of muscle exercises. In our experience, even when religiously prosecuted, these have proved futile in the cure of the truly pronated flat foot. In the main, the failures have been attributed to lack of co-operation but the fact that pronation may occur even in the presence of a well developed musculature seems to have been overlooked. Despite this, and possibly in deference to the natural reluctance of parents to submit their children to surgery for relief of what appears at outset to be a relatively innocuous affliction, the conservative treatment has been maintained and by some extolled.

That the affliction is not so innocuous, nor the conservative treatment so effectual is indicated by the variety of surgical procedures which have been devised from time to time. Moreover the very multiplicity of the suggestions is in itself proof that no single method of surgery has thus far adequately solved the problem. Practically almost every important bone muscle ligament, and joint of the tarsus has been surgically attacked. Generally speaking the procedures employed fall into two categories—the anterior operations directed toward correction of the depressed longitudinal arch and the posterior directed toward inversion of the pronated heel.

That one or another of the anterior group of operations may successfully correct a true *platus* need not be denied. But whether the correction of the anterior deformity can effect a correction of the posterior deformity by pressure from below may be seriously doubted. It is, in fact, the failure of such efforts that anxious procedures intended to supinate or invert the everted hind foot owe their origin. On the whole, the anterior group of operations has proved to be more successful in restoring the longitudinal arch than the posterior

group has been in overcoming the pronation of the heel. In retrospect, it appears that these results might have been expected because of the failure to correct the pronation deformity at the apex of its angle of deviation, the subastragular joint. The realization of the importance of the proper handling of this joint above that of any of the other tarsal joints in the treatment of pronated feet seems to be the very basis of the good results obtained by Clark and later by Zadel.

In part, some of the difficulty which has been encountered is due to the fact that two anatomically different situations have been grouped together as a single clinical entity. Anatomically the foot is a unit composed of a number of separate segments. Physiologically, the foot consists of two separate organs, the hind foot and the fore foot. *Pes planus* so describes a flattening of the longitudinal arch, that is, a change in anatomical relationship between fore foot and hind foot, and *pes valgus* a rotation of the hind foot in relation to the longitudinal axis of the superimposed leg. *Pes plano valgus* describes the combined form.

Obviously the cure of *pes planus* must be by surgical means which act across the mediotalar joints to stabilize the fore foot in relation to the hind foot while the cure of *pes valgus* must be effected across the subastragular joint so as to stabilize the hind foot in relation to the leg. In the absence of a stabilized hind foot, it is useless to discuss the problem of the longitudinal arch.

By comparison with the lower or a throoped forms, in which the arch is depressed and the os calcis everted, the human hind foot is supinated. Naturally, the development of the longitudinal arch has been associated with this inversion of the heel, and *active sup nation* has been considered the mechanism of its accomplishment.

Largely under the influence of Keith, who expressed the opinion that "with the maintenance of the normal arch, ligaments are not directly concerned" but that the longitudinal arch of the foot is dependent on properly and automatically balanced muscles in leg and foot, the belief has been propagated that the cause of flat foot is a muscle weakness. E. C. Morton, who stated

From the Hospital for Joint Diseases

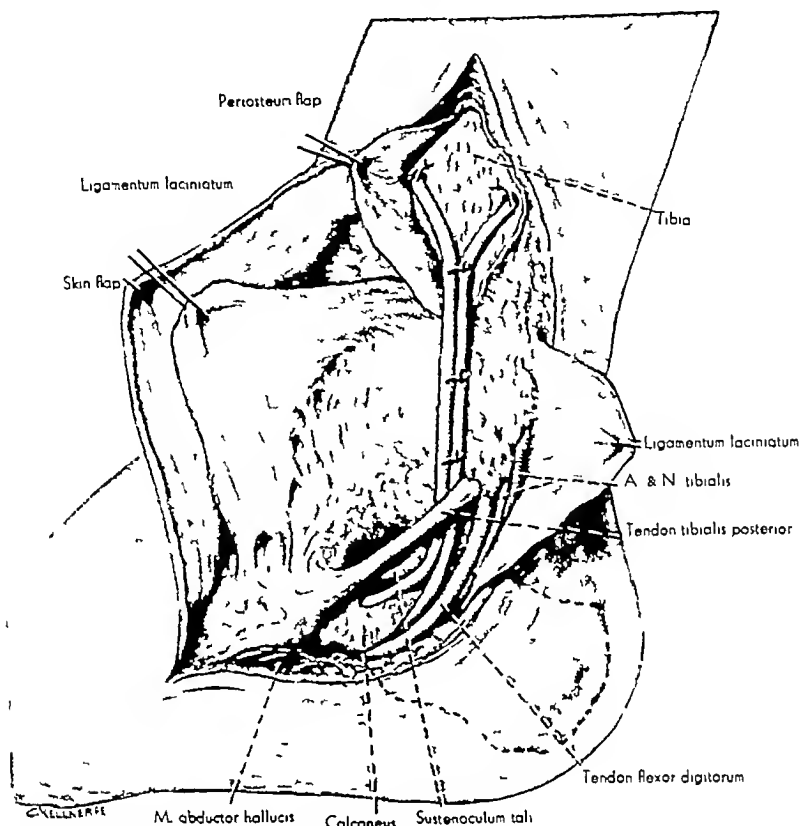


Fig 3 The fascial graft *in situ*, seen from the medial aspect. When sufficient graft cannot be obtained, the anterior ascending arm may be dispensed with.

is to prevent exactly that malposition which is characteristic of the pronated hind foot.

To simulate this action of the deltoid ligament, to elevate and invert the os calcis, the following operative procedure has been devised. Under a tourniquet placed around the calf, a curved incision is made, extending from the scaphoid tubercle backward around the tip of the internal malleolus and then upward to a point about 3 inches above the malleolar tip. At a point sufficiently above the epiphyseal line, to prevent injury to the growing zone, the medial surface of the tibia is subperiosteally exposed. A tunnel, running anteroposteriorly, is made, beginning on the medial surface of the tibia, above the epiphyseal line. Through this, a guide suture is passed. The incision is opened so as to expose the abductor hallucis below and the tendon of the tibialis posticus in front. The sustentaculum tali is visualized between the tendons of the tibialis posticus and the flexor longus digitorum muscles. With a broad, blunt, periosteal elevator, all the tissues lying below the sustentaculum and pos-

terior to the calcaneocuboid articulation are elevated, and a transverse calcaneal tunnel is drilled, so as to emerge on the lateral surface of the os calcis, in the region of the trochlear process. The guide suture previously passed through the tibia is now passed down along the inner aspect of the ankle, beneath the tendon of the tibialis posticus muscle, and around inferior surface of os calcis. A small external counter incision is made, and from without inward the graft is passed back through tunnel made in the calcaneus (Figs 2, 3).

A small incision is now made over the fascia lata, at the lower portion of the thigh. With the fascial stripper, a long strip of fascia is removed subcutaneously and is passed through the drill holes, exactly along the course of the guide sutures. The heel is strongly supinated and the strands of the fascial graft are sutured to the bone and are then united to each other, if possible. The wound is closed in layers and a plaster-of-Paris boot is applied, with the foot in the maximum of inversion. Immobilization is maintained for a period of 6 weeks. Upon removal of the



Fig 6 Case 2 Lateral view before operation



Fig 7 Case 2 Lateral view after operation

quently admitted to the hospital and on August 20, 1940, the right foot was operated upon, on September 3, 1940, the left foot was operated upon. The deltoid reconstruction operation described was performed on both sides, the heels being pulled into marked varus by means of fascial graft, and being maintained in this position by means of plaster of Paris boots for a period of 6 weeks. At the end of September, the plaster boots were removed and it was noted that the wounds had completely healed, but on the right side there was definite limitation of motion and evidence of a local inflammation. X-ray examination disclosed that this was due to some osteolytic lesion in internal malleolus.

This was, at first, thought to be due to pressure of the fascial graft against the underlying internal malleolus. However, the contour of the defect did not seem to be consistent with this interpretation, and re-examination of the preoperative x-ray films revealed some lesion which had been overlooked. Wet dressings were applied to the right leg, and in time the swelling subsided and a fair range of motion returned. On October 30, weight bearing was permitted, and shortly thereafter the patient was discharged from the hospital, walking in shoes with a wedging in the inner borders of the heels. On January 21, 1941, it was noted that both heels were in the neutral position. The longitudinal arches were well preserved and the prominence noted over the scaphoids had disappeared. The patient walked quite well, but on the right side some perimalleolar inflammation still persisted. On the left side, the range of motion at the ankle was excellent; on the right side, a slight residual limitation of motion persisted (Fig 5). Under physical therapy, this swelling gradually diminished and the range of motion in the right ankle increased. In June, 1941, it was observed that well formed arches were present on both sides. The feet were quite flexible, gait was normal, and the patient made no complaints. The arch supports were discontinued and patient permitted stock shoes with only small wedge along inner border of the heels. Up to present correction has been retained.

The second case proved of special interest because of the association of accessory scaphoids and markedly pronated heels. The accessory scaphoids caused no pressure symptoms and were neglected in the surgical procedure. The result obtained tended to confirm the opinion that the ligamentous repair was the essential element in the correction of the flat foot condition.

CASE 2 Mary R. aged 13 years, was brought to the hospital in the early part of September, 1940 because of flat feet and a painful prominence over the inner aspect of both feet which had been present for a period of about 2 years. Examination disclosed marked pronation of both heels, dropping of the longitudinal arches, and prominences over the scaphoids. The roentgenogram was reported as showing bilateral accessory scaphoids (Fig 6).

However, it was noted that when the heels were held in the varus position, the arches could be promptly restored. Because of this and despite the presence of the accessory scaphoids, it was felt that the pronation of the heels represented the primary deformity, and the operation here described was performed bilaterally. The postoperative convalescence was uneventful, and in the latter part of October, 1940, the plaster was removed. The wounds were found to be completely healed. The patient was fitted with Whitman plates and was then permitted to walk in wedged shoes. She was seen in December, 1940, at which time photographs (Fig 7) were taken. The patient noted complete absence of symptoms and restoration of well formed longitudinal arches. Foot plates were discontinued, and up to the present the arches have remained elevated. The accessory scaphoids are still present but do not appear to cause the patient any discomfort.

The procedure here outlined would seem to have its special application in adolescent patients between the ages of 8 and 14 or 15 years, in whom excessive pronation of the heel persisted. In younger children, the operation would probably present greater difficulties and might be unnecessary. In older patients, the definitive establishment of the tarsal joints would probably vitiate the result. In the proper age group, the procedure has the merit of being completely extra-articular and of avoiding the danger of injury to the epiphyseal growth zone. Thus far, the feet operated upon have remained flexible, painless, and with well formed arches.

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Fig. 4. Case 2, before operation. Note the medial concavity of the Achilles tendon. On the lateral view the prominent scaphoid tuberosity is clearly visible.

plaster a well molded foot plate is prepared and patient is allowed to bear weight in well edged shoes.

Since the operation is intended solely for those cases in which excessive pronation has resulted from a loss of the restraining action of the deltoid ligament, it is clear that it should not be employed when the pronation is caused by bony deformity. Obviously a "mushy due to a malunited fracture

of the lower end of the tibia is not amenable to correction by this procedure. It is essential therefore to determine by roentgenograms of the ankle joint that (1) the plane of the articular surface of the tibia is perpendicular to long axis of the bone, (2) the astragalus is held in its normal position by a well developed ankle mortise and (3) there is no abnormality in the os calcis. If these facts can be established, the pronation may be attributed to a loss of deltoid ligament support.

Theoretically the operation is applicable to all such cases regardless of age. However it would appear to be undesirable to attempt drilling of the os calcis before sufficient bone had been laid down to minimize the danger of interference with normal growth. Similarly it would appear unwise to defer operation beyond the time when a physiological readjustment of the tarsal articula-

tions might be reasonably expected. Quite arbitrarily therefore it is suggested that the optimum period for operative intervention is between the ages of 7 or 8 and 4 or 15 years.

The first of the cases treated by this method was operated upon in 1937. Usually a well formed arch in a thoroughly flexible foot has resulted. In general, the greater the supination of the hind foot, the higher has been the longitudinal arch. But even when the arch has not been completely restored the elimination of pronation of the hind foot has been accompanied by a marked relief of symptoms. There is usually complete relief of pain and the sense of fatigue present before operation.

The following case reports present special points of interest.

CASE. RAMON B. aged 9 years, was admitted to the hospital in August, 1940. At the age of 2, the child had been seen and treated at the hospital for bow legs. He was brought to the hospital at the present time by his parents.

He noted "prominent bones on the inner aspect of both feet." On examination it was noted that there was marked "algia" of both heels, especially the left, with pronation of both feet and flattening of the longitudinal arches (Fig. 4). At first it was thought the patient was suffering from accessory scaphoids or enlarged scaphoid tuberosities but x-ray examination showed no evidence of any abnormality in the scaphoid region. The patient was con-



Fig. 5. Case 2, after operation. On right, the supination of the heel is greater than on the left. On lateral view the arch on the right side is better than on left. The prominence of the scaphoid tuberosity has disappeared.

TABLE I—GEOGRAPHICAL DISTRIBUTION
193 CASES (SINCE 1913)

Geographical Unit	No of cases
North America	40
I rance	32
Eastern and Central Europe	31
Scandinavia	23
Germany	21
Italy	16
England	13
South America	7
Orient	4
Africa	3
Switzerland	2
Low Countries	2
	<hr/> 194

question appeared only with the publications by von Zoegge-Manteuffel (1898). Since his time a literature has accumulated that is not only large but increasing, due at least in part to recent accessions in the medical periodicals of North America and Central Europe. No effort has been made here to assemble a complete tally of all the cases published, and bibliographic efforts have been confined principally to the years since 1913. Faltin in 1902 found 79 reported cases, Ekehorn, in 1904, 92, Bunschuh, in 1913, 110, Kunz in 1928, 155, Podlaha, in 1929, 168. Taking Bunschuh's (1913) review as a basis, a cursory search of the readily available sources has yielded 194 cases (including the current one) since the date of his report. The total of 304 recorded cases is without doubt incomplete. The geographical distribution of the 194 cases collected is of more than mere statistical interest, in view of the geographical aspects of the etiology of the disease, which will be discussed later. It also shows that the incidence in North America is relatively greater than is generally assumed (Table I).

ANATOMICAL FACTORS IN ETIOLOGY

It has been accepted from the beginning that torsion of the right colon depends on an abnormal degree of mobility of cecum and ascending colon, this would make cecal volvulus basically a congenital disease, Lynch (1933) listing it as the most important of the abnormalities of the colon which require surgery. The anomalous freedom of the right colon¹ has been almost universally conceded to be an embryological accident, failure of obliteration of the fetal right mesocolon with the consequent persistence of an adult mesentery, though von Thun (1913) has suggested that general enfeeblement of the abdominal organs and acquired enteroptosis might also play a part.²

The sequence of events in the fetal abdominal cavity by which the colon gains its adult position and attachments is too well known to require detailed repetition here. It may be said, in brief, that the cecum gains its mature locus through the operation of three processes: rotation, which carries the originally left sided ascending colon across the abdomen, descent, by which the cecum sinks from a subhepatic situation into the right iliac fossa, fixation, whereby the right mesocolon is lost and the right colon made adherent to the posterior abdominal wall. Mobility of the cecum depends largely on the degree to which this last process extends. If fixation is incomplete, the cecocolon enjoys a greater or lesser amount of freedom of movement, it may retain its own proper mesentery, or, if the terminal ileum is loose, a common ileocecolic mesentery may result. Descent is substantially complete by the eighth month of fetal life (Hertwig, 1902, Keith, 1910), the cecum has then attained its adult position. Fixation proceeds thereafter, but the final peritoneal relationships are not fully established until about 4 months after birth (Harvey, 1918). The possibility of hypofixation is balanced by that of hyperfixation, in which the process goes to excess, yielding an entirely retroperitoneal cecum, and spreading at times to involve the normally mobile terminal ileum. General hyperfixation, of course, precludes any possibility of cecal volvulus. However, hyperfixation is often local (Carslaw, 1928), the principal sites being the beginning of the transverse colon (by the duodenorenal ligament) and the hepatic flexure (by the right renocolic ligament), though it can occur anywhere on the ascending colon. Such a point of local hyperfixation, combined with looseness of the proximal large bowel, provides an anatomical situation obviously favorable for a cecal volvulus—there being a mobile segment and a fixed spot to act as a hub.

A right colon which has failed to gain normal stability by fusion of its mesocolon with the posterior parietes is, nonetheless, often protected by the formation of secondary supportive attachments. Such structures as Jackson's membrane, Lane's band, and various pericolic membranes are to be explained on such a congenital basis (Connell, 1913, Gray and Anderson, 1913, Munroe, 1926). Flint (1921) has often seen a band anchoring the otherwise free cecum laterally,

quired not congenital. This is volvulus of the cecum alone about the long axis of the bowel. It can occur only in a cecum which has become secondarily pouched and distended. Pouching must be taken as an acquired cecal characteristic for the fetal cecum is a tapering one which merges imperceptibly into the base of the appendix.

¹It must be noted that the normally fixed cecum is usually free enough to be lifted out of the wound in the process of performing an appendectomy. Flint (1921) believes that study of cadavers is misleading on this point. This normal mobility is clearly evidenced by the x ray findings of Moody (1929). Engel (1857) ascertained that 70 per cent of ceca can be raised readily. Dreyer (1911) gives a figure of 67 per cent. The whole colon is much more mobile than many suppose. Barclay (1932) in fact would have it shifting about the abdomen under certain circumstances, in an acrobatic manner. Carson (1926) is of the opinion that real fixation of the cecum is entirely abnormal. The mobility with which we are here concerned—that which allows of cecal volvulus—is of quite a different order than the normal freedom.

²There is one form of volvulus usually considered rare, though Corner and Sargent (1905) think it may be common which is regarded as ac-

VOI VULUS OF THE CECUM

Anatomical Factors in Its Etiology Report of a Case

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VOLVULUS of the cecum, usually in volving to some extent the proximal colon and terminal ileum, is generally regarded as one of the rare causes of intestinal obstruction. Yet, on the basis of incidence alone, cecal torsion deserves more than passing notice. Lenormant (1929) found that 3.4 per cent of his 33 cases of intestinal obstruction were due to a twist of the right colon. Jacobsen (1934) analyzing 53 cases, obtained a figure of 11.6 per cent. Pratt and Fallis (1937) state that 5 to 6 per cent of instances of ileus in the United States is caused by cecal torsion; this percentage—which to the present authors, seems amazingly high—is challenged by Sweet (1935) who found only 1 per cent of 300 cases determined by this condition. Estimations of the proportion of cecal volvulus, as compared with volvulus of other locations, vary widely. Jacobsen (1934) states that 31.6 per cent of all cases of volvulus are of the right colon. Gushé (cited by Sauré and Lejeune, 1934) 7 per cent. Sweet (1935) 11.3 per cent.

There are other reasons for accordng this disorder serious consideration. Homans (1921) has noted that while it is less common than sigmoid volvulus, it is surgically more important than the latter. Moreover the mortality is high, exceeding 50 per cent. The need for early diagnosis and immediate surgical intervention in the usual acute case is emphasized by Chalfant (1931) figures of 96 patients operated upon, 59 per cent died of 23 not operated upon all died. The significance of cecal volvulus is further heightened by the possibility that, in addition to the acute cases ordinarily reported, there exist instances of chronic partial torsion. Twyman (1923) has recorded an example of the latter and considers it a

diagnosable entity. Such an opinion is supported by Corner and Sargent (1905), Pratt and Fallis (1937) and Grace (1938). In this connection, it is noteworthy that Berger (1933) in a study of 69 patients, found volvulus complete in only 42 per cent. It is possible that there is some relationship between partial cecal torsion and that much disputed entity *cecum mobile*. Finally it is clinically important that partial cecal volvulus may produce symptoms like those of acute appendicitis. Pascalis (1936) states that he has attended several persons with suspected appendicitis who were found at laparotomy to have a twisted right colon; he believes that cecal volvulus must always be considered in the differential diagnosis of diseases presenting signs and symptoms in the right lower quadrant.

DEFINITION

It is not easy to formulate a definition of volvulus of the cecum. As will be seen the abnormal anatomical freedom which permits the development of this disorder varies in degree. Therefore, volvulus, centering about the cecum runs the gamut from a twist of the isolated cecum to torsion in volving all of the small intestine and most of the large. The designation "volvulus of the cecum" is misleading; most of the cases so named involve also a variable amount of the ascending colon and terminal ileum. The condition could better be termed "volvulus of the right colon," were not the present name so firmly entrenched. Gettler, Mowbray and Forcher (1931) have proposed that "volvulus of the cecum" be defined as a condition in which torsion is limited to the cecum, ascending colon, and terminal ileum. This forms a satisfactory entity on embryological and anatomical grounds, since the right colon is usually fixed in its upper reaches, no matter how defective may be the peritoneal attachments of the cecum and adjacent bowel. Clinically this definition serves to separate right colic torsion from sigmoidal, ileal, iliac, and total volvulus.

LITERATURE

The first report of a case of cecal volvulus probably that of Rokitsansky in 1841. Critical considerations of the

Contribution from the Northwestern University Medical School, Department of Surgery and Department of Anatomy (No. 5 from the latter). Portions of this paper were presented before the Chicago Surgical Society, April 21, 1937, and before the American Association of Anatomists, April 24, 1937 (Abstract Anat. Rec. 91: 79. No. suppl. No. 7, 1937).

*Corner and Sargent (1905) computed a fatality rate of 60 per cent in 37 cases of patients operated upon and not operated upon, collected from the literature. Chalfant (1931) mortality figure of 6 per cent in 8 cases of patients operated upon and not operated upon. Berger (1933) death rate of 53 per cent in 69 cases of patients operated upon.

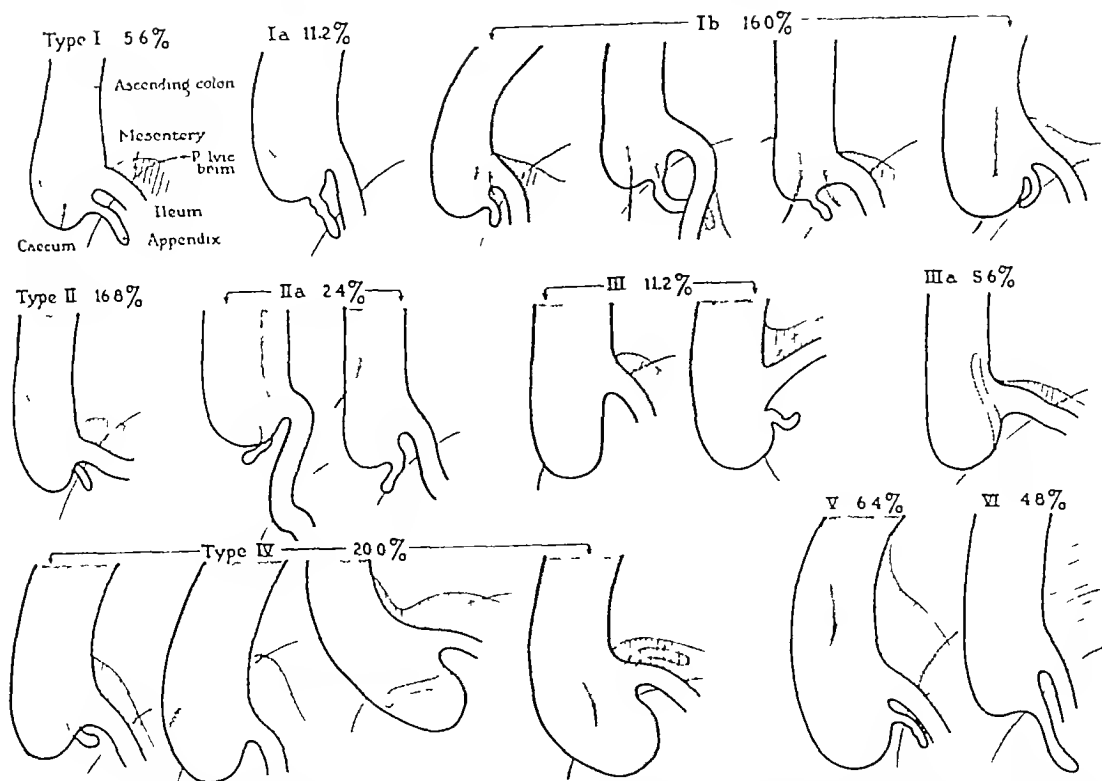


Fig. 1 Diagrammatic figures based upon actual specimens recording the range of ileocolic attachment in

125 consecutive adult specimens for convenience types are indicated the percentage occurrence of each type noted

occur in 14 subjects (11.2 per cent). In type III₁, the line of attachment ascends, leaving the cecum free, this arrangement obtains in 7 or 5.6 per cent. Figure 4 illustrates an example of type III₁a: a hyperdescended cecum hangs free in the true pelvis, with a line of attachment beginning just above the ileocecal junction and ascending colon without adhesion. In 25 instances, 20 per cent, type IV, this line of fixation is situated well above the ileocecal junction, though the cecum is sometimes fixed laterally by a descending line of fusion. In Figure 2 is pictured a cecum that falls into class IV. It is somewhat exceptional in that a redundant cecum, fixed in the iliac fossa, turned backward upon itself to point upward and touch the liver (termed an "erect cecum"). Figure 3 illustrates another example of type IV, in which however there are two extra retaining bands. In type V, 5 subjects, 6.4 per cent, the cecum and much of the ascending colon are free of attachment to the posterior abdominal wall. Figure 6 is an example: there is a completely mobile cecum and ileum as shown by the ease with which it could be retracted medially. The ascend-

ing colon is also without fixation throughout much of its length. Type VI, 6 subjects, 4.8 per cent, illustrates complete freedom of the whole right colon. Such cases have, to a greater or lesser extent, a common ileocecolic mesentery.¹ Figure 8 shows an example of this type, further complicated by a retroperitoneal ileum which occupied the iliac fossa, such an attachment would provide a fulcrum for volvular movement. Figure 9 illustrates another instance of type VI, it demonstrates that embryonic failure in rotation and descent is the basis of malposition, the cecum here occupying the left hypochondrium.

The application of these anatomical observations to the question of cecal volvulus is obvious. Only those right colons free of adherence to the posterior parietes for at least a part of their length are subject to torsion. It is immediately

¹Complete ileocolic mesenteric fusion does not occur as frequently in most series. Reeves (1909) found it in 2 of 125 cadavers, 1.6 per cent. Treves (1884) in 2 of 100, 2 per cent. Wan (1903) in only 1 per cent of 640 cases. Our criteria were perhaps more elastic: since we included all cadavers with a free cecal line, even if the hepatic falciform ligament adherent. All 5 of the 6 cadavers had a retroperitoneal ileum and 1 another a very short ileal mesentery, so that actually only 4 of 125 possessed a common mesentery.

while it has been Coughlin's (1927) experience that Jackson's membrane is present only in patients possessing an ascending mesocolon. An embryological explanation of the origin of these abnormal retaining membranes is afforded by assuming persistence of Reid's (1911) "genito-mesenteric fold." However, Croft (1930) would have it that if the cecum remains beneath the liver overlong, it acquires adhesions which persist even after fetal descent has taken place. Such secondary bands, if unsuccessful in immobilizing the cecum, become a menace to its integrity, since they achieve the same result as would local hyperfixation. In fact, the two processes may be akin.

While the failure of fixation is the principal cause of right colic mobility, it must be recognized that nonrotation and nondescent may also play a lesser rôle as early noted by Tandler (1897): the nonrotated or partially rotated cecum and the nondescended cecum are particularly likely to remain without effective fixation. The importance of these factors is indicated by the observation of Corner and Sargent (1905) that the left hypochondrium is the most common site of clinical cecal volvulus. Ruxford (1920) and Carter (1938) report cases of complete nonrotation (left sided colon) with subsequent cecal volvulus. Bulman (1924) cites an instance of embryonic failure in the midgut torsion (giving an hepatic flexure in contact with the splenic) which suffered a cecal volvulus. Some other accidents in the colon's development may also result in a free cecum. Thus the unique case of Low and Hilderman (1940) in which there was true hyperrotation (400 degrees instead of the usual 270) possessed a *cecum mobile* on a mesentery though there was no volvulus; it would have been anatomically possible. The rare occurrence of reversed rotation of the colon is evidently often followed by volvulus—cases have been reported in which patients died of their causes (Hunter, 1922; Harvey, 1926) while 3 cases have been recorded in which patients developed a cecal volvulus (Dott, 1933; Donald, 1927; Holman, 1940).

ANATOMICAL OBSERVATIONS

Stimulated by growing surgical interest in the ileocecal region, many anatomical studies have been made of the iliac and colic peritoneal relationships, some of them specifically directed toward the problem of cecal mobility. The present authors feel justified in adding another to this list of reports for 3 reasons: first, previous authors have often not examined their patients in detail before content to record some one fea-

ture second, many series have been concerned with children rather than adults; third, most of the exhaustive studies have been conducted in Europe, there being no comparable works in this country.

The authors have examined 125 normal consecutive adult dissecting-room cadavers. The mesenterial attachments of the cecum, ascending colon, and terminal ileum were critically studied; area of posterior fixation graphically mapped. In the records, however, no effort was made to distinguish between primary fixation and secondary attachments, or even between instances of common ileocecalocolic mesentery and those with a right mesocolon but which lacked continuity with the mesentery of the terminal ileum. A classification was then devised and the specimens were placed in the selected categories. Classification of the variations in the peritoneal attachments of the ileocecal segment incidentally is not clear cut, since in fitting cases into arbitrary types, the succession of almost imperceptible gradations in the extent of fixation must be disregarded. In Figure 1 are presented diagrams illustrating this classification and showing the distribution of 125 specimens among its types; each sketch was prepared from a specimen representative of the class, and, in some instances, demonstrating the scope of divergence within a class. Figures 2 to 9 contain detailed drawings of individual cases.

In type I (see Fig. 1) the cecum is completely or almost completely fixed to the posterior wall, being in some cases retroperitoneal. Seven specimens, 5.6 per cent, fell into this group. Figure 3 shows such a cecum, and illustrates the characteristic tight adhesion. In 4 subjects, 3.2 per cent, the cecum is attached through a third or more of its posterior surface (type Ia). In 20 cadavers, or 16 per cent type Ib, cecal adherence to the posterior abdominal wall, extending the length of the organ, is usually narrow in some instances being a very short mesentery. Type II is made up of specimens having peritoneal attachment at the ileocecal junction with the cecum free; there are 2 of these, 1.6 per cent. In 3 bodies, 2.4 per cent type IIa, the arrangement is complicated by tight adherence of the terminal ileum to the posterior wall. Figure 8, though not of a specimen belonging to type IIa, illustrates this type of fixation of the terminal small bowel. Cecum with a descending line of fixation beginning first at the ileocecal junction (type III)

*These were American subjects and specimens, mostly males, peritoneal dissection material of the anatomical laboratories of the Northwestern University Medical School. All were prepared for research by the phoshoxymercuric technique which leaves no noticeable stain on the body. Section with indications of some abnormality were reported.

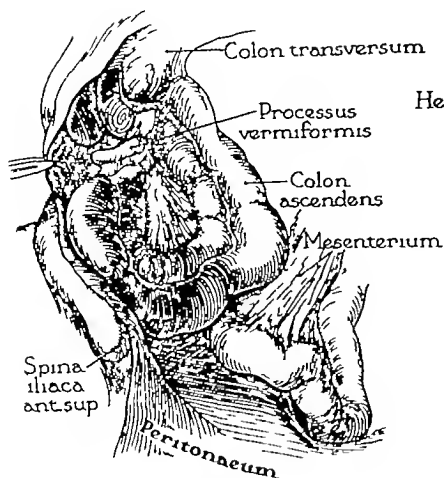


Fig 7

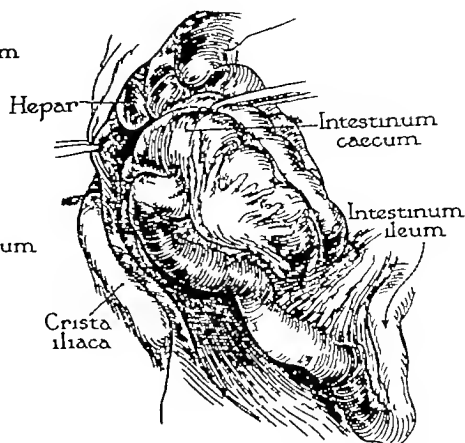


Fig 7a

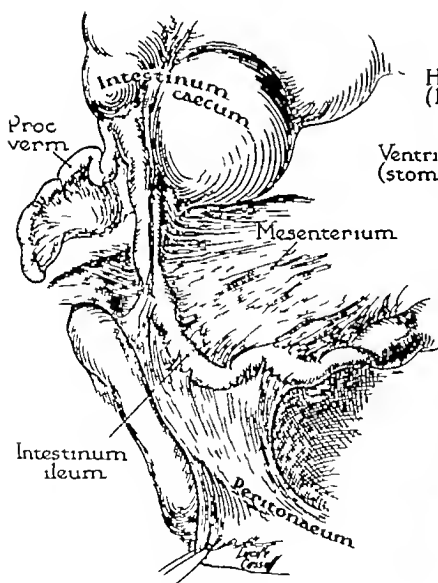


Fig 8

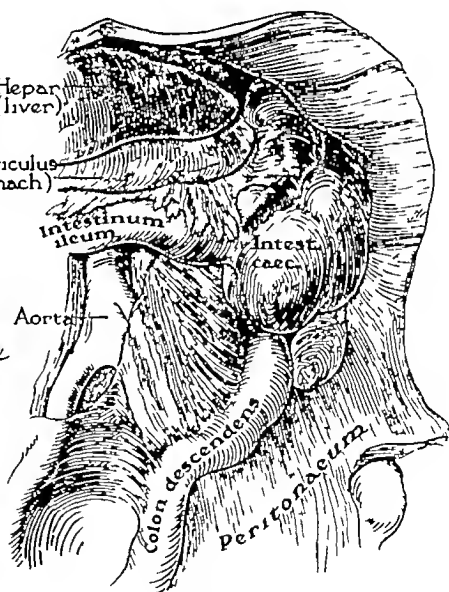


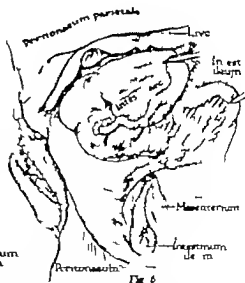
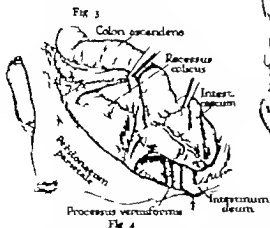
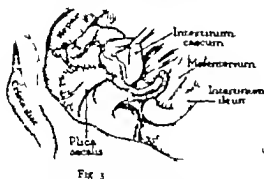
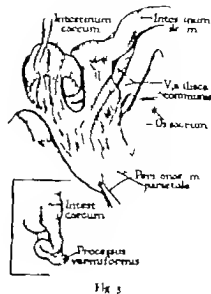
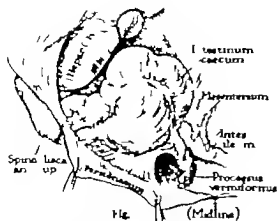
Fig 9

Figs 7 to 9 Drawings of cecum, etc, continued Figs 7 and 7a (same specimen), type V, Figs 8 and 9, type VI

could be manipulated into a position of volvulus in the abdomen of the cadaver. On the other hand, types V and VI are certainly predisposed to torsion of the right colon, all of the examples of these two classes permitted such manipulation. Type V would seem to represent the ideal in predilection, since in members of this group the bowel is mobile and the ascending colon fixed at a single locus which could behave as a stable

point around which the free segment could turn.¹ Three of the eight specimens of type V actually exhibited partial torsion. Figures 4, 7, and 7a illustrate a case in which the right colon had already been so rotated that the ileocecal junction

¹It is significant that many reported cases of clinical volvulus of the cecum were observed to have a band securing the ascending colon and acting as the hub of the twist. Lehmann (1922) reported a case of cecal volvulus in the presence of a free cecum and a retroperitoneal ascending colon and was able to collect 6 other cases from the literature.



Figs. 1-6. Detailed drawings of cecal and related structures from selected specimens. Figs. 1 and 2, type IV

Figs. 3 and 4, type IV. Figs. 5 and 6, type I

apparent that types I Ia and Ib are too firmly fixed to permit volvulus. Cecae of types II, IIIa and IIIb also seem too securely moored to permit twisting unless the cecum were to become greatly pouched. Even in the latter event a fixed point for torsion would be a further requisite. In this

particular class IIIa would perhaps be predisposed to volvulus because of the presence of a well anchored ileum. Types IIIa and IV in some instances present cecae that could revolve with concomitant pouching and dilatation to occur none of the specimens in these two categories

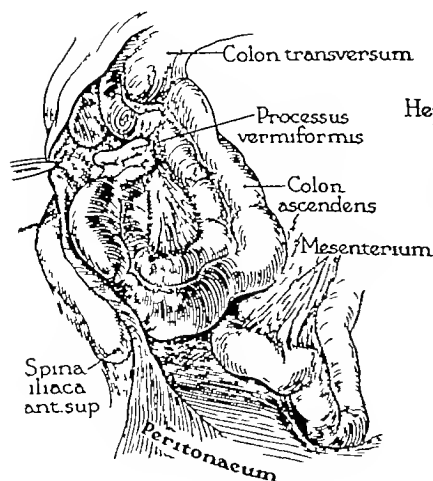


Fig 7

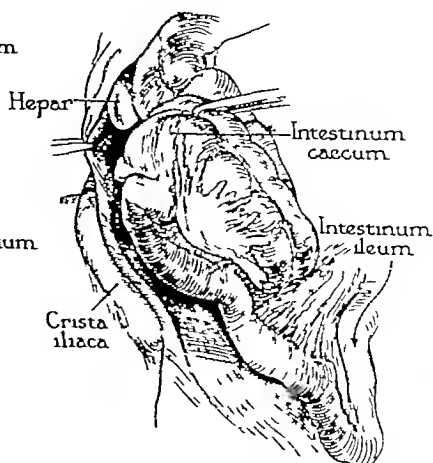


Fig 7a

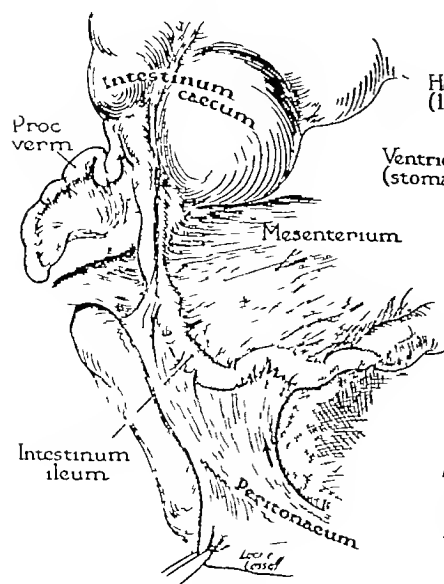


Fig 8

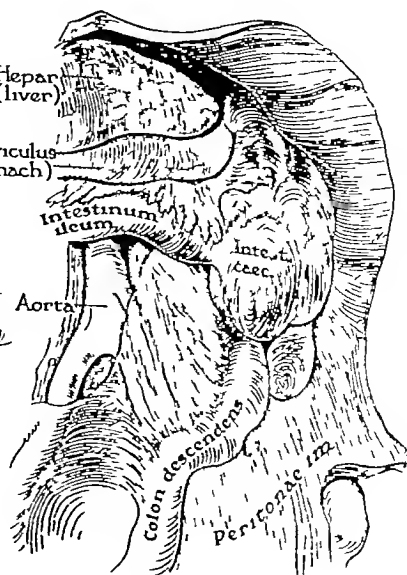


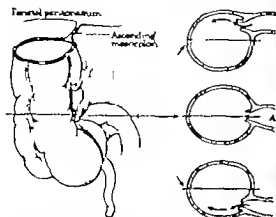
Fig 9

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The Hypothetical explanation, recorded in diagrams of the dependence of the direction of rotation upon the plane of the ileocecal orifice: the direction of force could tend to initiate clockwise turn (B) or counterclockwise movement (C) if the cecum turned from coronal plane (A).

was on the lateral margin of the large intestine and the ileum passed behind the cecum, as shown by lifting the latter. Treves (1885) and Pernkopf (1928) reporting cases similar regarded them merely as instances of unusual cecal position.

Types V and VI together making up 11.2 per cent of the series, represent the percentage in which the right colon is physically able to undergo twisting. This total perhaps should be added those which if secondarily pouched, could revolve. If volvulus occurred in members of types V and VI it would be truly congenital volvulus in members of other classes would be in a certain sense acquired.

A comparison of our figures with those of other investigators is given in Table II. It should be noted that these data were collected in various ways (for the possibility of maneuvering the cecum into a position of volvulus for the occurrence of right mesocolon, etc.). Some used cadavers others autopsy material or radiographic records; some studies were carried out on children others on adults. The figures in Table II are therefore not altogether comparable. It is significant that the incidence of ascending mesocolon runs over 20 per cent while that of extraordinarily mobile right colon is only 10 to 15 per cent—a fact that would indicate that a right colonic mesentery may be compensated for by secondary anchoring membranes. The present authors figure of 1 per cent of ceca able to form a volvulus compares well with Engels (1857) 10 per cent, Wandell's (1903) 10.3 per



The Roentgenogram of the sigmoid case, taken pre-operatively after barium enema. The cecum (toward lower left) is greatly dilated; arrow points to the end of the small intestine (the listed portion), through the latter barium reached the terminal colon and cecum.

cent Kantor and Schechter's (934) 10.4 per cent Treves (1885) 11 per cent, Harvey's (918) 3 per cent, Piernols (1907) 14 per cent, Alglave (1907) 15 per cent, and well also with Thurn's (913) 9 per cent. The higher figures recorded by some workers possibly may be due to the inclusion of infants, or to the failure to regard secondary bands of attachment. All in all it would seem fair to say that some 10 to 15 per cent of adults are anatomically predisposed to cecal volvulus.

In 1905 Kelly and Hurdon called attention to the fact that the terminal ileum may be firmly fixed even retroperitoneal, instead of normally free. Since then others have reported on various features of such cases (Oelachlegel 924 Benzel,

It should be noted here that anatomical information on presumed attachments of the ileocecal system are of service in other clinical matters than cecal volvulus. These attachments are of obvious importance to the symptoms of acute enteritis and of the possible pathological effect of retroperitoneum of this area as well as to such problems abnormal location of the vermiform appendix, internal hernia and ileocecal intussusception. Such latter fact Lynch (1911) and others point to be dependent upon clinical considerations. The book includes descriptions of such cases, no doubt having direct relation to the proper prognosis of ileocecal intussusception in the early years of life.

TABLE II—MOBILITY OF CECUM AND RIGHT COLON

Author	Date	No.	Mobile No	Per cent	Type of data	Description
Engel	1857	100	10	10	Cecum free	Adults
Treves	1885	100	11	11	Cecum free	Adults
Addison	1900	40	6	15	Ascending mesocolon	Adults
Wandel	1903	640	66	10.3	Able to twist	Adults
Alglave	1907	100	15	15	Cecum mobile	Adults
Piersol	1907	35	5	14	Cecum mobile	Children
Smith	1911	982	319	32.4	Ascending mesocolon	Infants
Dreicka		640		23	Ascending mesocolon	
Fallon	1913	100	22	22	Ascending mesocolon	Adults
von Thun	1913	388	72	19	Able to twist	All ages
Harvey	1918	105	14	13	Ascending mesocolon	Infants
Pirie	1920			20	Ascending mesocolon	Children
Bailey				25	Ascending mesocolon	
Begg				25	Ascending mesocolon	
Coughlin	1927	100	22	22	Ascending mesocolon	Adults
Kantor and Schecter	1934	383	40	10.4	Cecum mobile	X ray study of adults
Authors	1941	125	14	11.2	Able to twist	Adults

TABLE III—INCIDENCE OF FIXED TERMINAL ILEUM

Author	Date	No	Fixed No	Per cent	Description
Addison	1900	40	8	20	
Armstrong	1921	50	2	4	Cecum free
Alglave	1907	100	13	13	Cecum fixed in 8 per cent
Harvey	1918	105	9	8.6	
Leveuf	1914			10	Fetuses
Mollison and Cameron	1908	50	5	10	
Authors	1941	125	13	10.4	Adults Cecum free in 5 fixed in 8

such a segment is noted by Homans (1921). This particular type resembles those cases in which sigmoid volvulus is due to a similarly redundant sector.

THE MECHANICS OF CECAL VOLVULUS

Much has been written on the mechanics of cecal volvulus, and many classifications have been proposed, of which perhaps the best are those of Treves (1900), Corner and Sargent (1905), Faltin (1902) and McGowan and Dixon (1936). However, it is felt that too much stress should not be laid on classifications and rigid mechanisms. The literature amply demonstrates the simple fact that right colic volvulus can involve a variable amount of bowel, and that it can occur in many ways, depending upon the anatomical relationships and the presence or absence of pathological adhesions. Thus a colon with a common ileoceccocolic mesentery may turn about the superior mesenteric vessels as an axis, or, the opposite extreme, an isolated cecum may twist on itself—sometimes not obstructing the bowel, as in Makkas' (1929) case, in which the point of torsion was distal to the ileocecal junction. A locus of attachment on the ascending colon can act as the point of revolution and hence of obstruction, or a fixed terminal ileum can act in the same manner. If both the ascending colon and the ileum possess adherent areas, the intervening bowel can turn between them, if free, as shown in the patients discussed by Smith (1920) and Kirby (1929). A redundant loop of right colon with a narrow base can turn on itself after the fashion of a sigmoid volvulus, with obstruction of both the afferent and efferent limbs (Homans, 1921). Abnormal membranes or adhesions may further complicate the mechanism of volvulus, as in cases of adherent appendix (Nowland, 1925), of appendix fixed in the left pelvis (Cochrane,

1932, Piotet, 1934, LeVay, 1940). The importance of the fixed ileum in providing a point around which the right colon may swing to form a volvulus is noted in one of the cases of Sweet (1935), abnormalities of ileal attachment are stressed in this regard by McGowan and Dixon (1936). There have been a few studies on the percentage occurrence of fixed ileum, though the figures are at such variance as not to be very helpful (Table III), in these it is not generally indicated whether the cecum was free or fixed.² In our series, 13 subjects, 10.4 per cent, showed stable terminal ileum, whether retroperitoneal or bound down by extra bands, but only 5 of these, 4 per cent, were combined with a free cecum. The figure of 10.4 per cent compares well with the observations of previous authors, except for the low figure of Armstrong (1921) and the high one of Addison (1900).

No example of the rarer conditions (reversed rotation, left sided colon, hyperrotation, etc.), sometimes responsible for mobility of the right colon, was met with in the current study, nor was any case found in which the cecum and hepatic flexure were fixed and the right colon free and redundant between them. Volvulus of

²Armstrong (1921) reported two cases of fixed ileum with mobile cecum; he notes that two similar cases were found in a survey of 50 bodies.

1929) or even to the sacrum (Edwards, 1917). There are other rare and bizarre mechanisms, as for example Wistinghausen's (1919) case in which the terminal ileum wrapped around the ascending colon to form a pedicled cecum that underwent torsion.

The direction of rotation of an ileocecal volvulus cannot be completely accounted for on anatomical grounds. Many assume that the direction of twist is almost always clockwise. However as pointed out by Beeger (1923) and Graham (1926) direction depends upon how the cecum is placed and it is apparent from some descriptions and figures that not all authors have faced the hypothetical timepiece in the same direction. Beeger and Graham feel that the direction should be taken from an imaginary timepiece placed, dial upward, upon the patient's abdomen. Since many of the accounts in the literature are uninterpretable because of this confusion, no attempt has been made to compute the percentage of rotation in one direction or the other. Faltin (1902-1903) found only 15 of 50 analyzed cases had a clockwise twist. Jacobsen (1924) reviewing 24 cases, found 50 per cent clockwise. Von Zoega-Mantouffels's original idea that the medial attachment of the mesentery accounts for the usual clockwise rotation must be held in abeyance. It seems more plausible, mechanically for a free cecum to roll medialward on its mesentery than for it to turn counter clockwise beneath that structure. However Dixon and Miller (1940) are of the opinion that cases with a common ileocecal mesentery twist in a counterclockwise direction, while the turn is more frequently clockwise if the colon distal to the cecum is fixed. It is possible that the position of the ileocecal junction, dorsal or ventral to a frontal plane through the long axis of the right colon, may be important, since the force of the fecal contents driven against the anterior or posterior wall of the cecum might be sufficient to give the impetus for rotation counterclockwise or clockwise, respectively (Fig. 1).

INCITING ETIOLOGY

Although the anatomical background of cecal volvulus can easily be demonstrated, the fact that there are so few cases of the disease indicates that the inciting etiology deserves careful examination. That the anatomical predisposition is not the sole basis is suggested by a number of facts. Thus, von Thun (1913) found a majority of cases of cecal mobility in children below 5 years yet most clinical volvulus occurs in young adults. As a second point it should be mentioned

that there are cases in old persons who have anomalies obviously present since birth. Third, Bryant (1921) states that there is more marked ptosis of the right colon (and hence presumably greater mobility of the cecum) in females than in males, yet clinical cecal volvulus is recognized to be more frequent in the latter sex.

It seems evident that there are many causes of volvulus. It would be desirable to differentiate between those which merely set up a more favorable mechanical situation and those which actually set the process in motion unfortunately in the present state of our knowledge it is not possible to distinguish between the two. A large number of the causes listed in the literature seem to be of the mechanical variety. Many cases have been reported following events essentially traumatic, among them being exercise, heavy lifting, blows to the abdomen, coughing, jumping, dancing. Pregnancy seems to be an important mechanical cause of volvulus. Dreyer (1911) illustrates the manner in which the rising pregnant uterus displaces a mobile cecum (that such displacement occurs is confirmed by the radiographic studies of Eldering (1932) and Foeth and Ohlsson (1928). Pratt and Falls (1927) however believe that pregnancy causes volvulus not so much by mechanical means as by the abdominal peristalsis accompanying the vomiting of pregnancy. Surgical operations of different sorts have been followed by volvulus, and various kinds of intra-abdominal pathology have been cited as contributory in individual cases. Corner and Sargent (1905) state that the cecum is frequently found in the strangulated or obstructed right inguinal hernia of children and, when distended with gas, is almost always twisted.

There have been many summaries as to the possible etiological roles of such general factors as race, sex, age, country and diet. There is little evidence that cecal volvulus is of greater incidence in any particular race. The case for geographical influence is no stronger. In the early literature many of the victims were German (2 of Bundschuh's 110 collected in 1913). Later however Allpaw (1925) collected 39 Russian cases, Jacobsen (1924) analyzed 24 cases from Denmark, and several series of cases were reported from other Scandinavian countries. Podlaha (1926) collected 168 cases from Germany, Finland, Russia, Poland, and Scandinavia. Recently there has been an increase in the number of cases from North America, Central Europe, and France (Table I).

On the basis of circumstantial evidence, diet seems to be the most significant general factor

Pratt and Fallis (1927) and Ohman (1924) note that there was a large increase in the incidence of volvulus in the Baltic states during the Great War, when the diet consisted largely of coarse vegetables. Graham (1926) calls attention to the potato and sour bread diet of Finland and the vegetable diet and heavy eating in czarist Russia. The recent increase in the number of reported cases in America does not seem to have a dietary basis.

Cecal volvulus is conceded to be a disease of young adults. Corner and Sargent (1905) found 50 per cent of cases in the 20 to 40 year group, while Bundschuh (1913) met with 82 of 102 cases under 40 years, and 20 over that age. Faltin (1902) estimated that 71.4 per cent of his cases were less than 41 years and 45.4 per cent in the 17 to 30 year class. This is not in close accord with the anatomical evidence for the age incidence of mobile cecum, von Thun (1913) found that 51 per cent of bodies below the age of 5 had ceca free enough to produce a volvulus, 9 per cent of persons from 5 to 50 and 13 per cent of persons over 50 years of age.

There seems to be a definite sex predilection, males are more often affected with the disorder than are females. Pratt and Fallis (1927), analyzing 150 cases, found males predominating over females in a ratio of 3 to 1, while of Bundschuh's (1913) 110 collected cases, 76 were in men, and of Corner and Sargent's (1905) 57 cases, 42 were in men. Faltin (1902) found that 56 of 79 cases were males. This, again, does not fit in well with the anatomical facts, since it has been generally found that in males the right colon is less free than in females. Thus Harvey (1918) found a right mesocolon in 6 per cent of male infants and in 20.4 per cent of female infants. Wilms (1908) and Klose (1909, 1911) feel that *cecum mobile* is definitely more frequent in the female. Bryant (1921) makes a similar observation. However, Wandel (1903), whose large and carefully studied series demands respect, finds that, as regards ceca free enough to rotate, the proportion is slightly in favor of males.

It is a well known clinical fact that many cases of cecal volvulus occur without assignable cause, particular or general, some begin in the physiological quiet of night. Many cases have a prior history of long standing intestinal complaint. Heavy eating, constipation, and diarrhea have also been noted in cases of volvulus. One must therefore look to physiological maladjustments for the inciting etiology which plays on an anatomical predisposition. True, a mass peristalsis might constitute a true mechanical cause,

but upsets of normal peristalsis must be considered physiological in their inception. That the normally placed and fixed right colon is the site of complicated physiological activities, and that disturbances may easily upset their harmony has been emphasized by Homans (1921), such disturbance perhaps results in unusual amounts of putrefaction, in the formation of gas, misdirected peristalsis—leading in the end to distention, kinking, and volvulus. Perazzo, Zavaleta, and Artuso (1938) think that many of the so called traumatic and mechanical causes really act indirectly by setting up pathological peristalses. Harttung (1922) stresses constipation and anti-peristalsis as the cause of the actual torsion. McConnell and Hardman (1922) find differences between peristalsis in normally and imperfectly fixed right colons. It should be mentioned that some think a rôle is played by the ileocecal valve in the causation of cecal volvulus (Perazzo, Zavaleta, and Artuso, 1938). Amazing as it may seem, the physiology of this structure is only now beginning to be understood (Wakefield and Friedell, 1941).

CASE REPORT

Mrs. M. N., a white female, aged 71 years, entered Passavant Memorial Hospital August 16, 1938, on the service of Dr. Howard B. Carroll.

On the evening of August 14, at 5:30 p.m., she ate some honey dew melon and shortly thereafter experienced abdominal distention. At 9 p.m. she began to have generalized abdominal cramps. She took a half bottle of magnesium citrate, which was followed by six watery stools, which did not, however, relieve the pain or distention. On the morning of August 15 she took another half bottle of citrate of magnesia and later a Seidlitz powder. Orange juice, lemonade, and paregoric were taken, but all were vomited. Pain and distention continued. There were two watery bowel movements during the day. The pain, distention, and vomiting continued up to the time of admission on the 16th.

The past history was not pertinent except for constipation of many years' duration. She avoided fried foods, white sugar, white flour and desserts, and had lost 15 pounds in the past year. "Pills" and mineral oil had been used for constipation for many years.

Physical examination revealed a thin woman, with normal pulse and temperature and a blood pressure of 160-90. The head, neck, and chest were normal. The abdomen was markedly distended, tympanic over the dome, and dull in the flanks. There was no rigidity, but there was generalized tenderness upon palpation. No peristalsis could be seen. The left lower abdomen bulged, and palpation revealed a mass in this locus. The red blood count was 4,580,000, the white blood count, 4,500, the hemoglobin, 14.0 grams. A differential blood count showed 62 per cent polymorphonuclears, 30 per cent lymphocytes, 8 monocytes. The urine contained three plus albumin and some granular casts.

A diagnosis was made of intestinal obstruction, very likely a volvulus. The patient was given intravenous fluids and hot abdominal packs. Her vomiting abated and she passed a fairly comfortable night. There was no stool and she passed no flatus. The distention persisted. On August

7th day as given barium enema. A large mass of barium was seen in the lower abdomen, with an area of constriction in the lower right colon (Fig. 3). The patient was seen by the senior author on the afternoon of August 7 and was operated upon soon after.

When the abdomen was opened, through right lower abdominal incision, some blood-tinged fluid escaped from the peritoneal cavity. Loops of ileum were found to be distended. The ascending colon was collapsed, but in the lower abdomen and pelvis could be felt large, distended loop of intestine. The dilated segment, on delivery from the peritoneal cavity was made up of the cecum and the first portion of the ascending colon. There was a 90 degree clockwise twist. The dilated loop was some 6 inches in length, 7 in diameter. Its wall as so thin that the contents of the lumen could be distinguished. The loop was untwisted, catheter implanted, and the cecum emptied of 1/2 liters of fluid. A larger tube was then implanted for the purpose of colostomy. There was no evidence of necrosis. The gut was replaced and the abdomen closed. The operation was well tolerated. After operation constant gastric aspiration was applied and also suction to the colostomy tube.

On the following day the patient condition excellent, and convalescence went smoothly until the 5th postoperative day when she seemed sicker and demonstrated dependent edema. Her blood chlorides were found to be 400 milligrams per cent and she was given transfusion of 300 cubic centimeters of citrated blood.

On the 6th postoperative day she displayed respiratory embarrassment, and oxygen was administered. Her abdomen became distended, and fluids given by mouth did not pass the pylorus. She gradually became sicker and ran fever up to 103 degrees F. The chest became filled with rales, and she died on August 17 days after the operation.

At autopsy the cecum was as found to be of normal size and adherent to the anterior abdominal wall. There was no evidence of leakage around the colostomy tube. An acute fibrinous peritonitis with pockets as demonstrated, judged by the pathologist to have been due to proptosis, ending. There was also an acute bilateral fibrous pleuritis with hydrothorax, subtotal pulmonary arteriosclerosis and other relevant findings such as early partial cirrhosis, enlargement of the spleen, chronic cholecystitis with cholelithiasis and arteriosclerosis.

There are several points of interest in the case. One is the advanced age of the patient though by no means the oldest case on record, this is one of the most aged. Second, is the fact that a pre-operative diagnosis was made on the basis of clinical findings. Third, is the attributability of the fatality to the 2 day delay in seeking medical aid and the additional delay in resorting to surgery. This case serves well to stress the point that volvulus of the cecum, in its usual form, is an acute surgical emergency. The presence of a distended cecum is a constant menace through its thin walls contamination of the peritoneum can easily take place, as occurred in this patient, to prejudice seriously the success of inevitable operation.

The direction of torsion in this case was definitely clockwise in the sense defined by Beerger (1923) and Grabau (1926). The anatomical

mobility of the cecum was clearly evident. The loop was filled with fluid, not with gas, as Weinstein (1938) and Homans (1921) have assumed to be the case, because of the colonic anaerobes growing in an oxygen deficient milieu. In the current case however there was a narrow lumen at the site of the twist, which allowed barium introduced into the colon to enter the twisted loop (Fig. 1).

The inciting etiology in this case would seem to be pathological peristalsis, whether before or after the intake of cathartics cannot be stated. The diagnosis was made on clinical grounds, but confirmed by radiological examination. A scout film of the abdomen and a barium enema are of great diagnostic assistance. If a small lumen is present the volvulus can be directly visualized. If torsion is complete the point of obstruction shows up as a cone-shaped, smooth shadow. In such event, the presence nearby of a large dilated loop of bowel suggests cecal volvulus.

Prompt surgical intervention is necessary as emphasized by the case of Valentine and Kinross (1937) in which death occurred in 5 hours. The presence of vascular obstruction sufficient to cause necrosis cannot be determined unless the abdomen is opened. Leakage from the thin walled and distended cecum is a source of constant danger. The procedure to be utilized varies in the hands of individual surgeons. Many operations have been recommended, but, since these patients are usually debilitated, the simplest possible measure should be chosen. Untwisting and colostomy constitute the conservative procedure in cases in which the gut is viable. Patients having necrotized bowel, the involved sector can be exteriorized. Resection is used but would seem too severe an operation for any patient not in unusually good condition. The situation is quite different with regard to chronic or partial volvulus. In this contingency it is permissible to restore normal peritoneal relationships by some of the recoplastic procedures.

SUMMARY AND CONCLUSIONS

Over 300 cases of volvulus of the cecum have been reported in the international literature. It therefore follows that cecal torsion is not a mere surgical curiosity but possibility which should be kept in mind in the differential diagnosis of disease presenting in the right lower quadrant of the abdomen, and in the differential diagnosis of intestinal obstruction. The literature pertinent to the subject is briefly outlined.

It is proposed that volvulus of the cecum be defined as torsion limited to the cecum and adja-

cent terminal ileum and ascending colon, as suggested by Gatellier, Moutier and Porcher (1931). It is further proposed that the direction of twist be noted as clockwise or counterclockwise as referred to an hypothetical watch placed dial up on the patient's abdomen, as originally suggested by Beeger (1923) and Graham (1926).

In 125 normal adult cadavers studied consecutively by the present authors it has been demonstrated that in 11.2 per cent the cecum is mobile enough to allow the development of a volvulus. A survey of the literature indicates that 10 to 15 per cent of ceca are free enough to undergo torsion. In the present series 10.4 per cent of terminal ileums were found to be fixed, of these 38.5 per cent were associated with free cecum, and in these cases the attached ileum could serve as a hub were the ileocolic part of the digestive tube to revolve.

The anatomical arrangement which best predisposes to cecal volvulus is believed to be one in which the cecum is free and the ascending colon fixed somewhere along its vertical course. It is noteworthy that many accounts of clinical cases describe a band which binds down the ascending colon. Of 8 instances of this anatomical type encountered in the present authors' series of 125 specimens, 3 displayed some degree of torsion. The mechanism of volvulus varies greatly, but seems to depend chiefly upon the anatomical relationships and upon the position of fixed point or points for twisting.

The inciting etiology of this disease may be purely mechanical, or may be due to as yet incompletely understood physiological faults in the complex functioning of the right colon.

A case of cecal volvulus is reported. A study of this case serves to emphasize the necessity for prompt surgical care, and the importance of early examination by roentgenographic means. The authors suggest that cecostomy or exteriorization is the procedure of choice in acute cases, final selection depending on the viability of the bowel. Resection should be reserved for patients whose condition is very good. Cecoplastic procedures are permissible for chronic or partial volvulus.

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7th day as given a barium enema. A large mass of barium was seen in the lower abdomen, with an area of constriction in the lower right colon (Fig. 1). The patient was seen by the senior author on the afternoon of August 7 and was operated upon soon after.

When the abdomen was opened, through a right lower abdominal incision, some blood-tinged fluid escaped from the peritoneal cavity. Loops of ileum were found to be distended. The ascending colon was collapsed, but in the lower abdomen and pelvis could be felt large, distended loops of intestine. The dilated segment, on delivery from the peritoneal cavity was made up of the cecum and the first portion of the ascending colon. There was 90-degree clockwise twist. The dilated loop was some 6 inches in length, 7 in diameter. Its wall was so thin that the contents of the lumen could be distinguished. The loop was incised, catheter implanted, and the cecum emptied of 35 liters of fluid. A larger tube was then implanted for the purpose of cecostomy. There was no evidence of necrosis. The gut was replaced and the abdomen closed. The operation was well tolerated. After operation constant gastric aspiration was applied and also suction to the cecostomy tube.

On the following day the patient's condition was excellent, and convalescence went smoothly until the 5th postoperative day, when she seemed weaker and demonstrated dependent edema. Her blood chlorides were found to be 400 milligrams per cent and she was given transfusion of 500 cubic centimeters of citrated blood.

On the 6th postoperative day she displayed respiratory embarrassment, and oxygen was administered. Her abdomen became distended, and fluids given by mouth did not pass the pylorus. She gradually became weaker and ran fever up to 101 degrees F. The chest became filled with rales, and she died on August 7, 7 days after the operation.

At autopsy the cecum was found to be of normal size and adherent to the anterior abdominal wall. There was no evidence of leakage around the cecostomy tube. An acute fibrous peritonitis with ascites, as demonstrated, judged by the pathologist to have been due to preperitoneal seepage. There was also an acute bilateral fibrous pleuritis with hydrothorax, subtotal pulmonary infarctions and other relevant findings such as early portal cirrhosis, enlargement of the spleen, chronic cholecystitis with cholelithiasis, and arteriosclerosis.

There are several points of interest in the case. One is the advanced age of the patient, though by no means the oldest case on record, this is one of the most aged. Second is the fact that a preoperative diagnosis was made on the basis of clinical findings. Third, is the attributability of the fatality to the 2 day delay in seeking medical aid and the additional delay in resorting to surgery. This case serves well to stress the point that volvulus of the cecum, in its usual form, is an acute surgical emergency. The presence of a distended cecum is a constant menace through its thin walls contamination of the peritoneum can easily take place as occurred in this patient, to prejudice seriously the success of inevitable operation.

The direction of torsion in this case was definitely clockwise in the sense defined by Beegeer (923) and Graham (195). The anatomical

mobility of the cecum was clearly evident. The loop was filled with fluid, not with gas, as Weinstein (1938) and Homans (1921) have assumed to be the case because of the colonic anaerobes growing in an oxygen deficient milieu. In the current case however there was a narrow lumen at the site of the twist, which allowed barium introduced into the colon to enter the twisted loop (Fig. 11).

The leading etiology in this case would seem to be pathological peristalsis, whether before or after the intake of cathartics cannot be stated. The diagnosis was made on clinical grounds, but confirmed by radiological examination. A scout film of the abdomen and a barium enema are of great diagnostic assistance. If a small lumen is present the volvulus can be directly visualized. If torsion is complete, the point of obstruction shows up as a cone-shaped, smooth shadow. In such event, the presence nearby of a large dilated loop of bowel suggests cecal volvulus.

Prompt surgical intervention is necessary as emphasized by the case of Valentine and Kinner (937) in which death occurred in 5 hours. The presence of vascular obstruction sufficient to cause necrosis cannot be determined unless the abdomen is opened. Leakage from the thin walled and distended cecum is a source of constant danger. The procedure to be utilized varies in the hands of individual surgeons. Many operations have been recommended, but since these patients are usually debilitated, the simplest possible measure should be chosen. Unwinding and cecostomy constitute the conservative procedure in cases in which the gut is viable. In patients having necrotized bowel, the involved sector can be exteriorized. Resection is rare but would seem too severe an operation for any patient not in unusually good condition. The situation is quite different with regard to chronic or partial volvulus. In this contingency it is permissible to restore normal peritoneal relationships by some of the osteoplastic procedures.

SUMMARY AND CONCLUSIONS

Over 300 cases of volvulus of the cecum have been reported in the international literature. It therefore follows that cecal torsion is not a mere surgical curiosity but a possibility which should be kept in mind in the differential diagnosis of disease presenting in the right lower quadrant of the abdomen, and in the differential diagnosis of terminal obstruction. The literature pertinent to the subject is briefly outlined.

It is proposed that volvulus of the cecum be defined as torsion limited to the cecum and adja-

HAZARDS OF FIRE AND EXPLOSION OF ANESTHETIC AGENTS

III In the Presence of Diathermy

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THIS report, the third in a series on the fire and explosion hazard in modern anesthesia, is best viewed as a logical development of our previous reports. It is especially related to the paper on cautery ignition (3), which we recommend for study before reading this report.

The application of high frequency electrical currents to surgery is widespread and increasing, it is practically indispensable in some phases of modern surgery, especially neurological and genitourinary surgery. Therefore, anesthesiologists must accept the presence of electrosurgical apparatus in the operating room and must adapt their methods to this hazard.

Paralleling the increased use of electrical instruments in the presence of anesthetic agents and equipment is the decreased use of open ether and chloroform volatilized with air, and the greater utilization of semiclosed and completely closed methods of administration of ether, ethylene, and cyclopropane, with high concentrations of nitrous oxide or oxygen, or both. While these changes have been of great value in diminishing intraoperative and postoperative morbidity, they have, unfortunately, augmented the likelihood of serious injury to the patient and the surgical team exposed to an anesthetic combustion. It is more important than ever before to prevent anesthetic ignition, especially the entirely preventable types associated with electrical apparatus.

A marked discrepancy and a lack of unanimity in anesthetic practices exist with regard to these dangers. Even in hospitals with otherwise progressive departments of anesthesiology, we have found unsafe techniques in use. Many have adopted inadequate compromises as a result of incomplete understanding of the details of the hazard, e.g., barring ethylene and cyclopropane but allowing ether (17), or forbidding combustible inhalation anesthetics in head and neck electrosurgery but permitting them in surgical diathermy.

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employed at more remote points of the body or extremities (5).

It is high time that there be established a universally accepted standard of safe practice of anesthesia with diathermy. We believe that our studies have secured sufficient information to make this possible, and more, to make it convincing.

ELECTRICAL DATA

The basic information about combustible anesthetics has been presented in detail in foregoing reports (3, 4). All that is necessary, we believe, to secure understanding and agreement with our opinion on this type of electrical hazard is a presentation of the electrical aspects of high frequency apparatus as they are related to the possibility of igniting a combustible inhalation anesthetic mixture.

The heat necessary for ignition—182 to 517 degrees C. (3) may be considered present whenever a visible or audible spark is produced. For practical purposes, this is a necessary and safe rule even though it might be shown that there are degrees of sparking which cannot ignite anesthetic mixtures (we do not know of any such proof). When the surgical diathermy is employed, sparking or arcing may appear in five zones: (1) at the active electrode during fulguration, coagulation, or cutting, (2) within the cabinet of the apparatus if the machine has a spark-gap or defective insulation, (3) at the foot or hand switch controlling the make and break of the circuit, (4) at the wall plug socket during the make or break of the connection, (5) *this is the one source of sparking usually overlooked*—at many scattered and unpredictable points where a high frequency current or induced current jumps an air gap formed between the patient (charged by the high frequency electricity coursing between the two electrodes) and a grounded conductor or any conductor of sufficient electrical capacity to accept a charge. Such a conductor may be a nearby grounded or ungrounded machine or person.

We must consider each of the five zones in greater detail with regard to explosion protection from the sparks arising in each zone.

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rection of regional blocks, spinal anesthesia, rectal basal narcosis, and intravenous barbiturate anesthesia now makes it safe and feasible for a trained anesthetist to administer a noncombustible anesthetic whenever high frequency currents must be employed.

Our personal experience is worth citing as typical of the necessary and practicable adjustments in anesthetic methods safe for use in the presence of x-ray and diathermy apparatus. In our early years, we were fortunate in our ignorance to have used, without mishap, ether-oxygen-nitrous oxide and cyclopropane-oxygen for fluoroscopic surgery and surgical diathermy in various parts of the body, ranging from the breast to the cervix. With further education and experience, we have learned to discard these dangerous practices and to substitute noncombustible methods without serious difficulty. An increased use of spinal and other regional blocks, intravenous barbiturates and rectal basal narcotics combined with nitrous oxide-oxygen or regional blocks has enabled us to supply noncombustible anesthesia whenever the surgeon has desired to use the x-ray or diathermy. And at no time were we ever doubtful of the safe control of the depth of the anesthesia. Our most common occasions for changing a combustible inhalation anesthesia to a noncombustible technique have occurred in radical breast and neurological surgery. In both, we have been well pleased by the supplemental use of minimal amounts of intravenous barbiturates injected into the tubing of the infusion usually started with radical breast and neurological surgery. Simultaneously, the combustible agent is removed from the apparatus and "washed out" of the patient. The inhalation apparatus is used to supply nitrous oxide-oxygen with relatively large amounts of oxygen (20 to 25 per cent) and to provide an accurate indicator of the respiratory excursions. We have found this combination of minimum doses of pentothal sodium with optimum oxygen-nitrous oxide the answer to most of our problems of supplying noncombustible anesthesia in the presence of diathermy, when spinal or regional block was impracticable.

CLINICAL DATA

We have found published warnings (7, 8, 16, 18, 19, 22) against the use of diathermy apparatus with inflammable agents as far back as 1924. Through the 16 years, it has been repeated again and again. Yet explosions and deaths have been caused by the practice even up to the present, and the hazard is being repeatedly tempted in very many hospitals, even by some of the largest

We believe that the reasons for this continued violation of safe practice are four, one or more of these accounting for the persistence of the dangerous combination in different institutions: (1) Ignorance—of the physics and chemistry of the subject and therefore of the reality of the hazard, (2) indifference—to the hazard because of past "blind" good luck and because of unawareness of the catastrophes experienced by others, (3) inflexibility—of available methods of anesthesia because of lack of versatility and training in the anesthetist, forcing the use of combustible anesthetics in hazardous circumstances, (4) conflict—of opinion among surgeons, anesthetists, and diathermy manufacturers, fostered by the lack of an official and unequivocal censure of the unsafe practice.

In the literature and in our discussions with many anesthetists and surgeons, we have noted an almost universal disregard or oversight of the "diffuse sparking" tendency of high frequency currents, a fact long known to physicists. We have found only two statements alluding to this feature, but both without explanation. Size (20) has stated "at the present time there does not seem to be any certain way of guarding against miscellaneous sparking from this procedure," i.e., diathermy. The Minister of Health for England and Wales, in a memorandum (14) on the use of electrical apparatus in the presence of an inflammable anesthetic, pointed out that the patient, under an electrical potential while in a surgical diathermy circuit, may allow a spark to jump from himself to the operating table or anesthetic apparatus.

The elimination of the first three of the reasons stated above, for the persistence of the unsafe practice of mixing diathermy with inflammable anesthesia, is entirely dependent on the universal elevation of the standards of education and supervision of anesthesia and anesthetists. Fortunately, this is rapidly, but not rapidly enough, becoming a reality.

Most authorities condemn the practice under discussion, but we have found several writers who have permitted the loophole to remain, through which the erring anesthetist may escape condemnation. These writers, usually on very inadequate grounds, have indicated that ether inhalation is permissible with diathermy. For example, Mock stated "The anesthetic of choice in these cases of goiter is 0.5 per cent procaine hydrochloride used locally. With this anesthetic no precaution need be taken on account of the electrical current. Nitrous oxide may be used without fear of an explosion, and ether can be used. In the lat-

1 The active electrode always produces a spark or arc whether the high frequency current is adjusted for fulguration and coagulation (which are visibly associated with arcing) or for cutting. This knife like action is performed, not by a hot electrode, but by an arc which forms ahead of the electrode and which separates the tissues by volatilizing them (2). The danger arising from the arcing active electrode is as obvious and as localized as that of the hot tipped actual cautery. All the rules suggested in our earlier report (3) on the cautery may be applied here. We refer the reader to this paper for details.

2 The sparks in the cabinet of the apparatus may be caused by the multiple spark-gap frequently used to produce the high frequency oscillating current. This source of sparking is absent in the type of equipment which substitutes radio vacuum tubes for the spark-gap mechanism. Another source of sparks may arise from faulty or worn insulation or loose contacts. All of these internal machine sparks may be rendered innocuous by following the same precautions as have been described for the active electrode or actual cautery. Another method of protection that has been employed is the placing of the machine outside of the operating room and using very long lead-in wires to the electrodes.

3 The sparking at the foot or hand switch is an obvious hazard easily removed by enclosing it in a bag through which it may be operated, similar to the suggestion made for the fluoroscopic foot switch.

4. The plug-socket hazard at the wall connection may be avoided by inserting the plug before the start of anesthesia and removing it only after the anesthesia has ended and the room well ventilated. To prevent accidental disruption of the connection, one should use a locking type of wall socket (21). Of course if the socket is located outside of the operating room, the above precautions are unnecessary.

5 The scattered and unpredictable type of sparking mentioned before in zone 5 cannot be surely and safely prevented as the following consideration explains. Arcs may be produced in the presence of high frequency generators under conditions that would be absolutely safe from any other form of electrical spark. There are two reasons for this. (a) Arcs may be drawn from a high frequency conductor by a grounded conductor or by any conductor of relatively high capacity, e.g. a human body even if it is perfectly insulated. In the case of an insulated body it is continually charged and discharged by electromagnetic induction and if the distance is small this electromag-

netic stream will cause ionization of the air in between to the extent of forming a continuous arc. (b) An otherwise well insulated conductor may acquire an induced high frequency voltage by being near a high frequency conductor. Arcs may then be drawn from it very easily as described in (a). Many substances which are poor conductors or even good insulators to direct current or low frequency alternating current are good conductors of high frequency electricity. All of these special characteristics observed in using high frequency increase in proportion to the frequency and the frequencies employed in surgical diathermy are very high.

This information shows how difficult it is to limit the path of high frequency electricity and the possible points of arcing. Even with the inactive electrode on the sacrum and the active electrode at the urethra the currents are traversing all parts of the patient and are not entirely confined to a narrow path lying between the electrodes. A current diffuses itself more or less throughout the body (11). This device route is followed partly because of the varying electrical resistances of the structures in its path. No matter how far the electrodes may be from the risk, the hazard of arcing in or near the insulation system is a constant threat.

The prevention of this diffuse type of sparking is possible theoretically by connecting the patient to all objects and persons likely to approach him closely. To offset the increased hazard of electric shock introduced by this greatly increased circuit and capacity it would be necessary to add a high resistance barrier between each person and any likely grounding contact. It should be apparent how difficult this would be. Much more so than the Horton system (9) of intercoupling described for the prevention of electrostatic sparking. For in addition to the group connected by the Horton intercoupler (operating table, patient, anesthetic, and anesthetic apparatus) it would be necessary to include in the circuit all of the surgical teams and instruments which might draw a spark from the electrically connected patient and group in the immediate vicinity of the anesthetic inhalation system.

It should be evident why we consider the use of a combustible inhalation anesthetic mixture as entirely unsafe in the presence of electromagnetic energy anywhere on the patient. Even with precautions theoretically possible but never applied and highly impracticable, the practice is not as safe, more cumbersome, and less practicable than the use of noncombustible anesthetic methods and techniques. The progress of anesthesiology in the di-

to 220 volt current to a metal part that is usually insulated or to the secondary circuit which normally carries only a very small amperage. If "grounding" is in use, the electrical shock and the short-circuit spark are increased. The presence of a megohm resistance, as in the Horton intercoupler, between the "ground" and the person "grounded" eliminates the possibility of shock to those in the intercoupled group but does not prevent short-circuit sparking. The surgeon or a nurse, who are usually not included in the intercoupled group, may still be badly shocked or killed if he or she is standing in leather-soled shoes (which are conductive) on a "grounded" floor.

To prevent short-circuit sparking or electrical shock, it is necessary to check regularly the insulation of the diathermy equipment (in fact, all electrical apparatus on a house current) by means known to every electrician with the aid of a megger. It requires vigilance, circumspection, and repeated inspection to employ safely the modern equipment of surgery. These virtues are rarely used in most operating rooms until after the first accident has been experienced.

CLINICAL DATA

We have recorded 20 cases of fires and explosions ignited by diathermy apparatus. Three cases involving ether-air caused no injury, 8 cases of ether mixed with high concentrations of a source of oxygen (nitrous oxide or/and oxygen) resulted in the death of 2 patients, the serious injury of a third patient and 3 bystanders, and the slight injury of a patient and 2 bystanders. One case of nitrous oxide-oxygen containing an unknown combustible seriously injured the patient. Two cases of ethylene-oxygen caused the death of 1 patient and in another the rupture of the urinary bladder with recovery following repair. Two cases of cyclopropane-oxygen occurred, with the death of 1 patient. There were 3 cases of surgical field fires: alcohol ignited in 2 with the death of 1 patient, and ether ignited in 1 instance with death of the patient.

The igniting spark appeared at the active electrode, where the threat is exactly identical with that presented by the actual cautery tip, in 14 cases. The detailed consideration of this type of obvious hazard would be only a repetition of our discussion of the cautery hazard, to which the reader is referred.

In the remaining cases, the igniting spark occurred in unexpected and unpredictable places in or near the respiratory path of the combustible anesthetics although both the inactive and active

electrodes were deliberately and probably effectively kept out of contact with the gases. In these cases (definitely in 4 cases, and probably in 2 cases) the spark was of the type which is less obvious and more difficult of prevention, namely, the "diffuse sparking" which has been described in paragraph 5 of the electrical data presented in the early part of this paper.

SUMMARY AND CONCLUSION

We have considered in detail the electrical basis of all sparking or arcing during the use of high frequency apparatus. The prevention of all sparks is impossible. The localization of the hazard to one restricted zone, as is possible with the actual cautery, is practically impossible. No matter how far from the mask the electrodes are placed, there is serious danger of spark ignition of a combustible inhalation anesthetic mixture. In view of the relatively narrow field of use of surgical diathermy and because of the practical impossibility of spark prevention during diathermy, we have reached the conclusion that combustible anesthesia is contraindicated by the surgical need for diathermy in any part of the head, neck, body, and extremities.

We have directed attention to the other hazards of surgical diathermy in the operating room, namely, surgical field fires, fulguration-produced explosions of hydrogen in the urinary bladder and electric shock and sparking resulting from short-circuits in defective apparatus.

Our study forces us to conclude with the bald statement:

Anesthetic fires and explosions ignited by diathermy, like those due to x-ray apparatus, are completely preventable only by the use of noncombustible anesthetic methods. Failure to use such methods in the presence of diathermy is an admission of inability to maintain the standards of safe anesthesia which have long been advocated by many authorities, which are here demonstrated as necessary, and which are now practiced in the better departments of anesthesia and surgery.

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ter 2 cases, a wet flannel roll is placed just below the lower edge of the mask and further protection against the fumes of the ether reaching the electric spark is provided by a rubber apron placed over the anesthetic frame and held tightly by clips against the skin of the cheeks and chin. If a general anesthetic is necessary rectal ether anesthesia, as in one of my cases, may be used. In all but one of the 15 cases in this series, local anesthesia was used. It is apparent that this author was recommending ether inhalation with electrosurgery of the thyroid gland without ever having used it.

Even the discoverer of the clinical usefulness of ethylene for anesthesia has committed the error of advising a combustible inhalation anesthetic with surgical diathermy. In 1924 Lockhardt and Kretschmer reported their use of ethylene anesthesia in 23 cases of fulguration of the urinary bladder and 1 case of carcinoma that received diathermy. In this article, they stressed the fire and explosion hazard of flame, cauterly and electric sparks. Then they described the careful placing of the spark-gap apparatus at a distance from the patient, with the machine cover kept shut and the lead wires to the electrodes drawn through holes drilled through the walls of the cover. Yet they failed to recognize the danger of the sparking active electrode and the greater threat of diffuse sparking from any part of the patient. No explosion occurred even though this was in the days of only semi-open administration of ethylene. This is an excellent example of the fact that failure to cause an explosion by violation of the rules of explosion prevention cannot be used as evidence of the harmlessness of the bad practice. An explosion is the result of the coincidence of many predisposing factors of which the absence of any one may prevent the accident is over by the many other favorable influences.

We have been surprised to find Guedel allowing Ethylene properly managed, may be used in electric fulguration within the bladder if the air bubble above the water is held to minimal size and the fulguration spark is not permitted to reach the bubble. (6)

Kovacs (2) in his authoritative textbook on electrotherapy has contributed to the indecisiveness of the warning against using diathermy with ether by describing its use in one paragraph, but, in the next, saying, "since however there have been occasional serious accidents resulting from ignition and explosion of ether . . . it is better to avoid its use when possible."

Kelly and Ward in their textbook entitled *Electrosurgery* repeatedly advised the use of the

hazardous technique of interrupted open ether anesthesia for oral and other types of surgical diathermy stating that the risk is slight with proper precautions, i.e., the patient exhales a few times and all ether-soaked materials are removed. While this was their most common method of general anesthesia, probably because of a lack of trained anesthetists, they admitted that rectal anesthesia administered by a trained anesthetist is the method par excellence.

Many manufacturers, in the commercial literature accompanying their diathermy apparatus (17) have warned against the use of ethylene but advised that ether might be used with only the precautions of an ether screen and wet towels. One of the leading manufacturers so poorly understood the ignition possibilities of diathermy that he considered the sparking hazard present only in the spark-gap type of machine and absent in the vacuum tube models.

The precautionary steps necessary to allow the change-over from a combustible anesthetic to a noncombustible one for use with diathermy are the same as are those which have been advised and described for cautery surgery. (3) about the need after a combustible inhalation agent has been used.

There are three other varieties of hazard of special interest: the anesthetist when the diathermy is operated in the surgery. (1) The active electrode can ignite an inflammable cleanser or antiseptic fluid painted on the surgical field as it did in 3 cases. In this respect, the cautery and diathermy present the same problems. The field and drapes prepared with an inflammable cleanser or antiseptic should be thoroughly dry before the active electrode is applied, or better yet, a noncombustible fluid should be used. (2) There is a type of accident peculiar to bladder fulguration during which hydrogen may be liberated by the decomposition of the irrigating water within the bladder. The hydrogen rises to the dome of the bladder, mixes with the air bubble, and is subject to explosion whether or not an inflammable anesthetic agent is in use. (6) (3) The last type of danger is that of electrical short-circuiting with the resulting effects of electrical shock and sparking. These are possibilities which are ever present.

If electrical apparatus of any type receiving its source of power from a house current (110-220 volts) The main line of current may reach the operator or patient or by accident or intentionally in circuit with a part of the apparatus which has become live because of a break in the insulation within the machine or a defect in a condenser. This allows a leak of the main line

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BACKACHE

THERE is an increasing tendency in this country to ascribe all lame back conditions to a ruptured intervertebral disc resulting in a herniation of its nucleus pulposus into the spinal canal, and when no evidence of such a lesion can be demonstrated by examination or by operation, there is a further tendency to make a diagnosis of a thickened ligamentum flavum. It must be remembered that pain in the back is still pain, and as such is only a symptom of many conditions which may exist in the back itself or regions outside the back, e.g., peptic ulcer, kidney and pelvic lesions, Hodgkin's disease, diseases of the blood (leucemia) and general infections. One of the most prominent and early symptoms of small pox is severe backache.

Low back pain above, or in combination with, radiating pain especially along the course of the sciatic nerve, may be present in a great many instances in which there is not a shred of evidence by x-ray or by myelogram of any local intraspinal lesion. It would be just as

logical to assume that all headaches are due to intracranial lesions. There are no typical physical signs of a herniated nucleus pulposus. Certainly a diminished knee jerk or absent ankle jerk is not pathognomonic, since these alterations may be seen in cases in which there has been a prolonged sciatica from many other causes. Furthermore, the removal of a herniated nucleus pulposus or a thickened ligamentum flavum does not always relieve or cure the lame back.

There are many conditions which may produce this so often distressing and even agonizing symptom, e.g., occupational attitude, sprains, compression fractures, malignancy, arthritic infections, local and general disturbances in the abdominal, pelvic, and retroperitoneal regions, pregnancy, relaxed abdominal walls after pregnancy, mechanical conditions of the extremities such as tilted pelvis, unilateral short leg, foot strain, contracted fascia lata, and bad posture. There is a large group of patients who may have severe pain radiating down the sciatic nerve. This pain may be alternating and the patients may show no clinical signs whatever of low back trouble. They are apt to be fascial, not "muscle bound."

On the other hand, a patient may have the severest of lame backs without any evidence by x-ray or other tests of any abnormality in his vertebral column, and the reverse of this is true, he may exhibit by x-ray marked congenital abnormalities or severe osteoarthritis of the spine and never have a lame back. When a patient does have a lame back in the presence of such abnormalities, why does he ever recover when these remain the same? There is plenty of evidence that recovery does take place and often without a recurrence of

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REVIEWS OF NEW BOOKS

IT is estimated that 40 to 50 per cent of all disease in man is due to infection. Approximately 250 living agents of animal or vegetable origin are known to produce disease at least 56 different bacteria, 8 spirochetes, 21 ultramicroscopic viruses, 63 molds, yeasts, actinomycetes, and pathogenic fungi, 16 protozoa, 31 helminths, and, about 51 anthropods. Infection involves two living entities—the infectious agent and the host. It is the balance between them which determines the outcome. A clinical understanding of the mechanisms of infection on one hand and of natural resistance and acquired immunity on the other is of fundamental importance in the prophylaxis and treatment of disease. On this thesis, Kolmer and Tuft have developed *Clinical Immunology, Biotherapy and Chemotherapy*,¹ which is composed of two parts.

Part I covers the general aspects of infection, immunity, biotherapy and chemotherapy while Part II is given over to the clinical applications of these principles which concern the diagnosis, prophylaxis, and treatment of disease.

The difficult and often confusing subject of immunology is presented in a clear, concise, orderly manner. A chapter is devoted to each of the following subjects: active immunization and vaccine therapy, passive immunization and serum therapy, bacteriophage therapy, methods of diagnosis and treatment of allergy, blood transfusion therapy, nonspecific protein therapy, and chemotherapy.

In Part II infectious diseases are grouped under suitable chapters, and emphasis is placed upon the immunological aspects of disease and treatment suggested along these lines. Such information is of greatest value to the student of medicine who has a fundamental knowledge of these diseases, as no attempt is made to present a complete clinical picture or to suggest general therapeutic measures. In most instances the authors have adhered to their subject and they have written with unquestioned authority.

The authors should be commended for editing this mass of material and correlating these related subjects in such an agreeable text. There is no other book known to the reviewer which contains such a wealth of material pertaining to the therapy and practice of immunology. Each chapter has a comprehensive summary and, in addition, to each a list of valuable references is appended.

HOWARD B. CARROLL

¹CLINICAL IMMUNOLOGY, BIOTHERAPY AND CHEMOTHERAPY IN THE DIAGNOSIS, PREVENTION AND TREATMENT OF DISEASE. By John A. Kolmer, M.S., M.D., Dr. P.H., Sc.D., LL.D., LL.D., F.A.C.P. and Louis Tuft, M.D. Philadelphia and London: W. B. Saunders Co. 1941.

THE book entitled *Surgical Diseases of the Spinal Cord*² by Elsberg is far too comprehensive to admit a discussion of any one specific feature of its many contents. It is in a sense a source book, yet a book which reads as easily as a good novel, and throughout the book one finds morsels of digression, such as a note on the history of laminectomy in Chapter VI, which enliven and enrich the text for the less intent reader. This work is noteworthy for its solid and conservative honesty, its lack of overstatement, and its easy avoidance of dogmatism. This is true because it is Dr. Elsberg's forthright statement of up to date factual data molded around his profound knowledge of diseases of the spinal cord resulting from his own vast personal experience. To illustrate this point one need but mention his opinions concerning the possible difficulties in the operative exposure of a ruptured intervertebral disc. The author certainly labors under no illusions, and he advocates the application of only solid surgical principles.

The book is beautifully printed. It is well organized as to content, it is well indexed, and the many simple half-tone illustrations enhance its attractiveness. Chapter X, concerning the diagnosis of cord tumors by clinical features at different levels, typifies the uncomplicated, direct, and effective style of the author. While it is definitely Dr. Elsberg's book, the chapters on roentgenology and pathology of diseases of the cord by Drs. Dyke and Wolf are worthy of the prominent place which they are given in the book.

Many contemporary surgeons will agree that Dr. Elsberg represents in relation to disease of the spinal cord that which Dr. Cushing did in relation to intracranial disease. As Cushing's contributions have been as yet but little enlarged and improved upon, even so, in the opinion of this reviewer, the American literature contains no current book surpassing this one in genuine reliability for student and clinician alike.

JOHN MARTIN

TO surmount the difficulties of making clear to beginning medical students the anatomy and function of the nervous pathways is one of the chief goals of every teacher of neuroanatomy. The subject must be presented in a simple fashion if it is to be remembered, and in simplifying it much detail, and possibly some accuracy, must be lost. Rasmussen is perfectly conscious of the shortcomings of a

²SURGICAL DISEASES OF THE SPINAL CORD, MEMBRANES AND NERVE ROOTS. SYMPTOMS, DIAGNOSIS AND TREATMENT. By Charles A. Elsberg, M.D. With chapters by Cornelius Dyke, M.D. and Abner Wolf, M.D. New York: Paul B. Hoeber, Inc. 1941.

satisfactory results began to be reported. Review of the history of colostomy from the time it was first recorded by Aurellanus as having been performed for ileus by Prazagoras, 400 years before Christ, down to the modern type of colostomy would be tedious and time consuming. Suffice it to say that Littré in 1710, through the medium of a child who died of a congenital obstruction of the rectum conceived the idea of a permanent colostomy although it was not until 83 years later that Duret performed a left iliac colostomy for a similar lesion. Another French surgeon Amussat established the principle of colostomy for rectal cancer.

Ward, in 1865 probably was the first to advocate routine lumbar colostomy in all cases of rectal cancer showing that the gradual recognition of this maneuver as an integral part of the treatment was slow in developing due largely to the refusal of the medical profession to accept an artificial anus.

As time went on mortality figures remained high and long range cures continued to result in only a small group of cases. Finally with the development of anesthesia, aseptic surgery and a better understanding of the fundamental principles of surgery as applied in this field it came about that Miles developed the technique which today unquestionably gives sufferers from rectal cancer a better chance of longevity than any other. Because the trend in the treatment of rectal cancer has been toward the Miles operation it is not perhaps amiss to note here that this extremely radical procedure which most master surgeons today recognize as combining the basic fundamentals of surgical attack on cancer of the rectum, is the result of the work of many men.

Czerny in 1883 performed the first one stage perineoabdominal resection of the rectum. Finding it impossible to remove a carcinoma well up in the rectum by the perineal route as planned, he promptly and courageously opened the abdomen and completed the resection transperitoneally.

From this time until the announcement of Miles monumental contribution to the surgery of rectal cancer many procedures have been tried and many modifications of Miles technique have been instituted, and it is a

tribute to Miles, Czerny and others who developed this operation that the trend both in America and on the Continent is definitely in its favor when it is at all applicable with reasonable mortality. The acceptance of colostomy as a step in surgery for rectal cancer is rarely now disputed. It is true that there remain a few surgeons who debate this thesis and who insist on attempting to perform a type of operation which will save the magnificent sphincteric mechanism of nature. To them I would venture the suggestion that a careful scrutiny of the end-results of such procedures is definitely in order and, I hazard the opinion, that comparison of a group of patients operated by this method with a group of patients receiving the advantages of a radical operation which includes colostomy will establish the superiority of the latter maneuver. I would not be understood as wholly condemning sphincter saving operations for indubitably if the cancer has not metastasized but is still local and of a low grade such a procedure may occasionally be indulged in with satisfaction. However I know of no way of actually determining prior to resection whether or not malignant cells have escaped to other parts and organs of the body.

Although radical operative procedures which remove areas of gland bearing tissues in the neighborhood of the original growth are always highly desirable it should be noted that one may not apply a single operative procedure routinely. A surgeon who is capable of performing only one technical maneuver for rectal cancer is not sufficiently versatile to combat the many difficulties which this type of surgery develops. Unquestionably the operation of Mummery which consists of colostomy and posterior resection has a definite field of usefulness in the armamentarium of all surgeons. Moreover I believe an occasional local excision because of reasons other than local conditions may be justified even an occasional segmental resection with anastomosis can be defended. All of which indicates that there are at least two operations, Miles and Mummery's, by which most rectal cancers may be operated upon and that there are several less radical procedures which, if included in

the surgeon's repertoire, will extend the field of operability advantageously

Surgery of the colon proper, necessarily awaited full development until the Listerian era, which followed the discovery of anesthesia and permitted fearless invasion of the peritoneal cavity

In the beginning colostomy as a decompressive measure was about the only operation performed for cancer, but gradually hardy and persistent surgeons doggedly extended the horizon and began attempts at removal of malignant lesions with re-establishment of the gastrointestinal continuity

As far back as 1823, Reybard, successfully resected the sigmoid flexure for cancer and made a primary anastomosis in a young man 29 years of age. Progress was slow thereafter, although Thiersch reported a resection of the colon for acute obstruction in 1843. Thirty-seven years later only 10 resections of the large bowel had been recorded and only 3 of these were successful. During the nineties, however, more resections were performed successfully because of the development of the principle of exteriorization

The discovery that a mobile segment of bowel harboring a cancer could be brought outside the peritoneal cavity and having the abdominal wall snugly closed around it remain *in situ* for subsequent resection marked an enormous advance in colonic surgery. This epoch making discovery decreased mortality figures hugely and gave great impetus to a field hitherto viewed with scant interest.

Many names are associated with this type of operation, and heretofore I have thought that Bloch, of Copenhagen, deserved credit for the first account of it published in 1891. However, I am now indebted to Dr John H. Gibbon, Jr., of Philadelphia, for some information which had escaped my attention.

In a paper before the American Surgical Society in May, 1941, he credits Thomas Bryant as being the first surgeon to bring a loop of bowel containing a carcinoma outside the abdominal cavity and suture the wound around it. Zachary Cope refers to Mr Bryant in his article entitled "Extra-abdominal Resection of the Colon".¹ The article by Mr

Bryant was published in *The Proceedings of the Royal Medical and Chirurgical Society* (London, 1882, 9: 149), and *The British Medical Journal* (1882, 1: 461).

Dr Gibbon also informs me that an American surgeon, J. M. Barton, of Philadelphia, published an article under the title "Cases of Abdominal Surgery, 13th Case, Resection at Ileocecal Valve for Epithelioma—Recovery" in the *Journal of the American Medical Association* (1888, 10: 549), describing a procedure which embodied the exteriorization principle. Subsequent to these resections, Bloch, in 1891, published a report of his type of resection.

In 1892, Recluse, collaborating with Forgeue, published a description of 2 cases of exteriorization of the bowel without mentioning Bloch's name. Paul, of Liverpool, 9 years later, published a modification of Bloch's method, by which he ligated the mesocolon, abutted the two limbs of bowel and decompressed the proximal loop with a glass tube. In 1902, Mikulicz spoke of the procedure which he claimed to have performed first in 1886, and for some reason his name has been commonly attached to all exteriorization operations by surgeons in this country. As a matter of fact, exteriorization represents the concepts of many surgeons, for a single isolated procedure only occasionally marks the discovery of a principle. Even more rarely is the discovery of a principle the work of one man, for research and recorded experiences combine to establish truth and exteriorization may well be said to be an ensemble of principles marking a new era in colonic surgery.

While mortality figures were enormously increased by the discovery of this principle, further progress was insured when the recognition of the principle of decompression prior to resection became universal.

Present day knowledge of the physiology of obstruction easily explains why a sick, dehydrated, and desiccated patient with an imbalanced blood chemistry is such a high risk for any formidable procedure. In consequence, it has come about that a period of preliminary decompression and rehabilitation has become a standardized practice in dealing with large bowel cancer. Such a period has for a long time been part of the attack on ob-

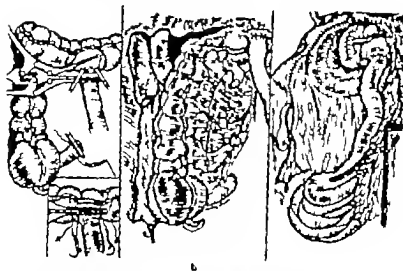


Fig. 1. The step in aseptic end-to-side anastomosis between the transverse colon and the terminal ileum. The anastomosis is made first as in a, and then division is made as in a one stage or two stage procedure. b, Shows mobilization of the right colon. The right kidney and duodenum are demonstrated. c, Shows completion of the operation with peritonealization of raw surfaces. An enterostomy has been done so catheters, from the anastomosis. This step may now be abandoned and the Miller Abbott tube inserted.

struction from gastroduodenal lesions, obstruction in the urinary tract, and other ailments which cause a profound physiological upset. Applied to lesions of the colon this principle has been no less emphatically advantageous and today it is an unwary surgeon who neglects this very necessary phase of the surgical attack.

When one is confronted with a combination of acute intestinal obstruction and cancer obviously disregard of the malignancy and attack on the acute intestinal obstruction is the proper sequence. How often this principle is modified or reversed in attack on the two ailments combined is an unforgettable error of judgment reflected in mortality statistics. Although cancer of the colon, particularly of the left colon in the vast majority of cases produces some type of intestinal obstruction, acute, subacute, or chronic, one may save in the acute variety always attempt medical decompression and with splendid chances of success. When the obstruction must be relieved surgically a cecostomy without exploration is the procedure of choice. This acute intestinal obstruction while usually due

to malignancy more than occasionally is the result of injudicious administration of opaque media by mouth a procedure to be entirely condemned as not only useless in the diagnosis of colonic lesions, but definitely dangerous in the presence of encircling neoplasms of the left colon.

Recently I have studied a group of cases of cancer of the colon and rectum which occurred in my private practice from February 1 1933, to February 1 1940. This group occurred in a series of 605 cases diagnosed as major lesions of the lower gastrointestinal tract. Of these major lesions 418 patients had cancer thus emphasizing the fact that practically 2 out of 3 of the major organic lesions of the colon and rectum are due to cancer. There were diagnosed 178 cases of cancer of the right and left colon 100 males and 78 females 170 were operated upon.

Table I shows the type of operation used for cancer of the colon, the resectability percentages, and the mortality figures. Operative technique and the question of type of operation must vary in the two halves of the colon because of differences in physiology pathology

TABLE I — ANALYSIS OF 170 CASES

Operations for cancer of the left colon	Cases	Deaths	Per cent Mortality
Obstructive resection and cecostomy (1 or 2 stages)	59	6	
Exteriorization	38	4	
Aseptic anastomosis and resection (cecostomy)	2	1	
Exploration alone or with de compression	37	3	
	136	14	10.2
Cases	136		
Operations	163		
Resections	98		
Operations for cancer of the right colon			
Ileocolostomy and resection, 1 stage	10	5	
Ileocolostomy and resection, 2 stages	14	0	
Colectomy and ileosigmoidostomy, (2 stages)	1	0	
Ileocolostomy	9	1	
	34	6	17.5
Cases	34		
Operations	49		
Resections	25		
Resectability		72 per cent	
Resectability		73.5 per cent	

and anatomy. As a general principle it is safe to assume that cancer of the right colon may be extirpated most satisfactorily by an ileocolostomy and resection in one or two stages.

Aseptic ileocolostomy between the terminal ileum and the middle of the transverse colon followed immediately or at a later stage by resection is the procedure of choice. My apostasy from an open type of anastomosis dates back 15 years or more when I developed an instrument for performing an aseptic anastomosis. In consequence, I am convinced of its utility in avoiding or at least reducing infection and certainly the simplicity of its performance recommends it to most surgeons. Nevertheless, in the modern management of colon cases and with the new chemotherapeutic agents available to sterilize the bowel, one may be quite justified in doing an open anastomosis if that is deemed preferable. An anastomosis between small and large bowel by whatever technique one chooses to do it is a relatively satisfactory procedure in so far as healing is concerned. The blood supply of the small bowel is copious, and that of the large bowel, while less free, is definitely adequate and usually of a constant pattern. Leakage at the anastomosis line is rare, and

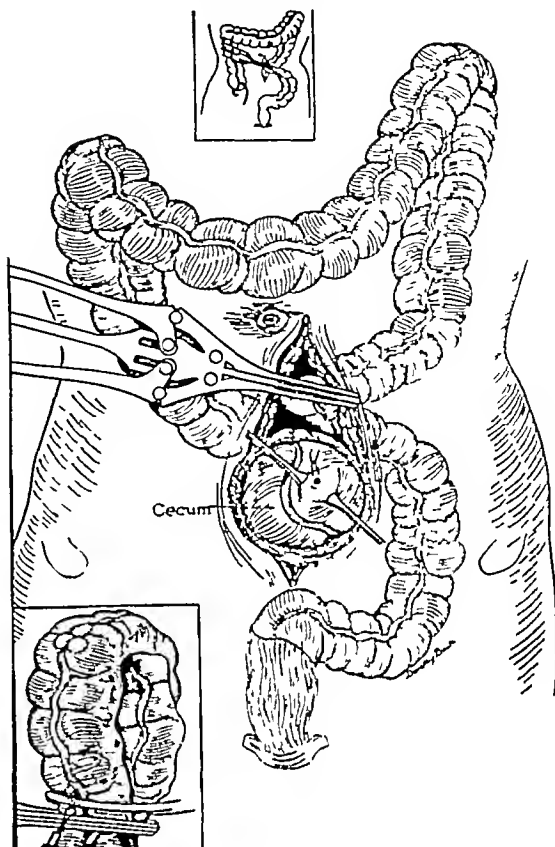


Fig. 2 Steps in obstructive resection plus complementary cecostomy. The addition of the cecostomy, which required very little time has been a very valuable adjunct.

when resection is done by modern types of technique is almost a unique occurrence.

Exteriorization procedures in the right colon I definitely deprecate for three reasons: (1) infection around the growth secondary to obstruction and ulceration is likely to produce a lethal peritonitis from the efforts at mobilization, (2) few circumstances are more unpleasant to a convalescent patient than a deluge of liquid alvine discharges over the abdominal wall, (3) it takes little extra time to do some type of anastomosis, and a patient who will tolerate an exteriorization will usually tolerate an anastomosis and thereby avoid the unpleasantness of an artificial stoma.

The mortality in the right colon in this small series indicates that a two stage procedure often is advantageous. In reviewing the 5 deaths which occurred following single

stage operation it is not apparent that a different type of technique would have resulted differently. One individual was an elderly person of 70 in good condition and with a freely movable right colonic cancer. She died 14 days after operation. Another individual was a middle age woman of 50, with 2 cancers, one in the rectosigmoid and one in the right colon. An ileocolostomy skelctracking the right colonic cancer as the first stage of a graded maneuver was performed. She died 3 weeks later of a subphrenic abscess. A third death in this series was due to leakage at the anastomosis.

Nevertheless I believe that there frequently are instances when it is desirable to use ileocolostomy and resection in one stage. More often I think it is desirable to do the operation in two stages. A question of ileostomy for decompression after primary anastomosis and resection seems to be satisfactorily solved at present by the utilization of the Miller Abbott tube. This tube does all that ileostomy can do and even more and avoids the unpleasantness of ileostomy as well as additional surgery.

In the left colon it will be noted that the choice of operation was obstructive resection and cecostomy. Usually the cecostomy is employed as a complement to the resection. Occasionally when a patient has an obstruction it is utilized prior to resection as a decompressive measure. In 59 patients operated upon by this maneuver there were 6 deaths and a mortality of 10.1 per cent.

I have been reticent to accept the principle of primary anastomosis in lesions of the left and transverse colon because the mortality in my hands has been higher and I have not been sure that I could do as radical a resection and immediate anastomosis as by resection and delayed union. I have no quarrel with surgeons who choose resection and primary anastomosis and feel sure that it is frequently indicated when the preliminary efforts at decompression have been adequate. On the other hand, I think the crux of the situation lies in the radical removal of mesentery and adjacent gland bearing tissues.

In considering immediate restoration of intestinal continuity economic factors must not

be allowed to influence surgical judgment, nor must the desire to perform an artistic surgical operation be considered favorably against a radical even mutilating type of procedure in dealing with cancer.

In this group of cases the resectability figure was 73 per cent. To improve the horizon of operability and to remove every cancer of the colon possible one must accept border line cases. Surgical removal of 3 out of 4 cancers of the colon accepts this principle as a necessity. The mortality figures in the right colon of 17.5 per cent are too high. On two former occasions I have reported mortality figures of less than 15 per cent for a series of right colonic cancers removed surgically. The latter figures should be accomplished in the hands of most surgeons without difficulty and will be possible, I think, if the graded procedure is accepted in all cases of cancer which are not freely movable or are complicated by local or general conditions. Certainly in order to do a one stage procedure one must select only the most favorable cases for resection. The mortality figures in the left colon were 10.1 per cent, with a resectability figure of 72 per cent.

Table II is an epitome of the entire group.

TABLE II.—OPERATIONS FOR CANCER OF THE RIGHT AND LEFT COLON

see Males	% Females
Total cases right and left colon, diagnosed	78
Total cases right and left colon, treated	70
Total operations	
Total mortality per cent	7

Many maneuvers permit a wide range in selecting a type of operation for radical extirpation for cancer of the colon and rectum. The cardinal principle of wide removal of the growth and the tissues in immediate juxtaposition to it as well as lymph gland bearing tissues situated more distantly is of course the ideal sought. Any type of operative procedure which gives a high percentage of ultimate cures must take into consideration the lymphatic system's relationship to metastasis.

The brilliant works of David and Gilchrist, of Gabriel, Bussey and Dukes, and of Collier Kay and MacIntyre are monuments to industry for they show beyond peradventure that

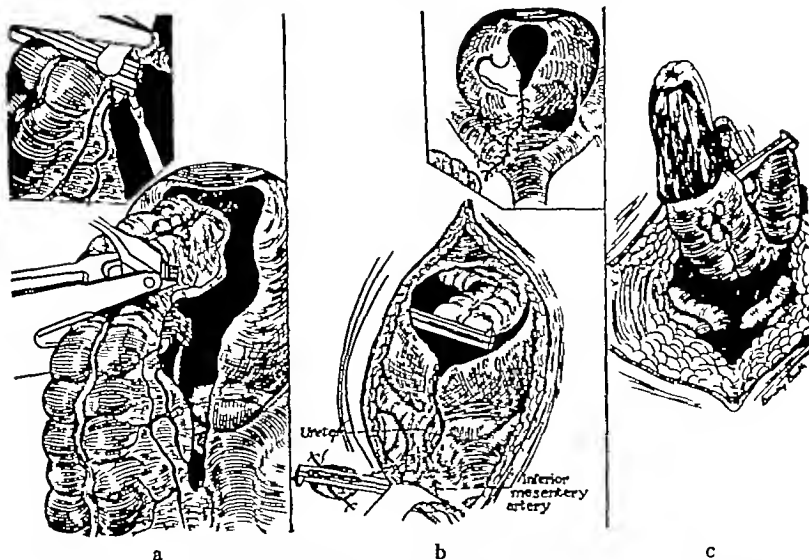


Fig 3 The steps in a combined abdominoperineal resection of the rectum in one stage a, Shows mobilization of the growth after ligation of the blood supply is completed. The pelvic dissection is shown completed and the Cope DeMartel clamp applied b, Shows the bowel and growth dropped back into the pelvis, a new floor being formed and the single barrel colostomy made through a stab wound in the groin c, The beginning of the posterior dissection. The rectum is mobilized up to the peritoneal fold and is then removed by this posterior approach

the more glands one inspects the more metastases one finds. Coller and his associates found that 60.8 per cent of all resections of the colon showed glandular involvement if a large number of glands were studied. Isolating an average of 52 glands per specimen, it was found that 59.4 per cent nodes showed malignant involvement, and 41.4 per cent were without metastases. Here again they emphasized a paradox which has long been recognized, namely, that a higher percentage of cancers of the right colon show metastasis than do cancers of the left colon. Actually 62.5 per cent of the cancers of the right colon in their series showed metastasis in comparison with 60 per cent of those of the left colon. Despite these figures more individuals who undergo operations for cancer of the right colon survive at the end of a given period than do those undergoing operations for cancer of the left colon. An explanation of this fact is not forthcoming, but statistics are definite on it.

David and Gilchrist in 1938, had a similar experience in dealing with cancer of the rectum. They found that in 68 per cent of rectal

cancers glandular metastasis could be demonstrated by a careful examination of a large number of glands. This work is supported by statistics from St. Mark's Hospital in London and has been buttressed by all investigators who have taken the pains to make examinations of large numbers of glands. It is established beyond any question of proof that widespread resection of the mesentery is necessary, consequently, a most important decision in choosing an operation for cancer of the colon comes, first, between graded and single stage procedures, and second, between immediate anastomosis and delayed union. There are surgeons who glibly assert that colonic resection should always be done in one stage, or on the other hand, two stages. Obviously there is a middle ground which is predicated upon the ability of the patient to undergo formidable resection in one operation, and the question of whether or not his condition will be advantageously treated by multiple procedures. Local conditions such as fixation, infection, and obstruction, and general conditions, such as age, obesity, and coexisting debilitating disease, decide the selection in the average

TABLE III.—CANCER OF THE RECTUM AND RECTOSIGMOID

275 Cases diagnosed 262 Cases treated			
75 Males	00 Females		
Diagnosis made	275		
Treatment given	262		
Males	275		
Females	100		
Disposition of cases	Cases	Deaths	Per cent Mortality
One stage combined abdomino-perineal resection	36	9	6.6
Two stage combined	7		
Colostomy and posterior resection	49	4	8
Posterior resection		0	
Radium	4		
Failure of Procedure			
Colostomy alone or with exploration	5	8	33
Exploration alone	10		
Cecostomy	3		
	262		

case. The final and ultimate decision will come only on exploration and individualization of cases at the operating table. Inevitably one must fit the operation to the patient and not the patient to the operation and such a program demands familiarity with many types of technical procedures.

There were 275 cases of cancer of the rectum 258 of which were operated upon 4 were treated by radium, and 13 refused operation or went elsewhere. In this group there were 175 males and 100 females.

In selecting an operation for cancer of the rectum, it is my confirmed opinion that there are few cases in which it is desirable to ignore the necessity of a colostomy as one of the steps of the operation. There are many reasons if one needs more evidence than the number of involved glands found in resected specimens why colostomy should be routinely employed. Certainly the burden of proof rests on those who would salvage the sphincteric mechanism to show that a comparable percentage of patients will be alive and free from disease in a given period of years. My own experience with the sphincter saving operations has been paralleled by that of many colleagues and may be summed up briefly in the statement that they usually are followed

TABLE IV.—OPERATIONS FOR CANCER OF THE RECTUM AND RECTOSIGMOID

	Cases	Deaths	Per cent Mortality
One stage combined abdomino-perineal resection	36	9	6.6
Colostomy and posterior resection	49	4	8
Posterior resection	1	0	
Colostomy alone or with exploration	53	8	15.3
Exploration alone	10		
T stage resection (Rankin)	7		
Cecostomy (acute obstruction due to cancer)	3		
	32	3	8.5
38 cases—(130 operations)			
193 resections			
93 resections			
36 one stage combined abdomino-perineal resection			
Resectability			74.8 per cent
Applicability			70.4 per cent

by recurrence fistula formation or stricture. It must be an extremely small percentage of cases of rectal cancer of low grade which have not metastasized and which are located favorably for local excision and segmental resection. This group in comparison to the whole is relatively insignificant.

Table III indicates the distribution of the rectal cancer cases treated in this series during the designated period. It will be noted that 13 cases were not treated by me. Of the group of 275 three of these were sent to me by colleagues for consultation and subsequently were operated upon by these surgeons. A combined abdomino-perineal resection of the rectum was successfully performed in each case. The 10 other patients went elsewhere for advice and treatment for various reasons. A few of these people refused operation because of my insistence upon colostomy as a part of the procedure. It has been my plan to hold fast to this principle. Occasionally patients do refuse.

Table IV shows the type of operation, mortality and resectability percentages as well as the applicability of the one stage operation in this series.

It will be noted that the trend in this series was definitely toward the one stage combined abdomino-perineal resection of Miles. Over a period of 15 years, I have found myself changing from a graded procedure in treating cancer of the rectum to a single stage opera-

tion wherever it is feasible—the reverse of practice in treating cancer of the colon. The advantages and disadvantages of a one stage combined operation are well known. A consideration of end results leaves few arguments necessary to establish the desirability of this radical one stage operation, but if further arguments were needed, the splendid work of David and Gilchrist and our English colleagues should convince the most stubborn that radical resection of a large portion of the mesentery of the sigmoid is definitely essential.

My own operation is useful only occasionally. When it is noted that I have performed it only 7 times in 262 operations its utility in a very small field is definitely established. Mummery's operation, while less radical than Miles, is a very useful procedure and should be applied to the less sturdy risks and to those individuals who for one reason or another are unable to withstand a formidable one stage operation.

The resectability rate in this series was 74.8 per cent. Of 258 patients operated upon 193 were subjected to resection of one kind or another. The applicability of the one stage resection to the whole group was 70.4 per cent.

This seems to indicate that with proper preliminary preparation one may apply the one stage combined abdominoperineal resection of the rectum not routinely, but at least with great frequency in any given series. The

mortality statistics show that the one stage procedure may be accomplished with a death rate comparable to that of other procedures. In 136 operations there were 9 deaths, a mortality of 6.6 per cent. This compares favorably with the group operated upon by the two stage procedure, 49 Mummery operations being performed with 4 deaths, a mortality of 8 per cent. The total mortality of the whole group was 8.5 per cent, with a resectability rate of 74.8 per cent.

Mortality statistics and curability figures are inextricably bound together and are influenced by many factors. Operability varies in the hands of different surgeons because of many circumstances peculiar to the surgeon and the case. Suffice it to say that it is a well recognized axiom that every effort should be made to extend operability curves which so vitally influence end-result percentages. Standardization of preoperative and postoperative measures as well as flexibility of the operative phase of the attack will no doubt still further reduce hospital casualties, morbidity figures and thereby enhance the satisfactory ultimate outcome. It is widely conceded that prognosis following successful radical extirpative measures for cancer of the lower gastrointestinal tract is satisfactory by present day standards. Nevertheless, the ultimate goal is far from reached and continued effort is essential to amplify efforts to combat successfully this modern scourge by surgical methods.

THE TREATMENT OF PATIENTS WITH SEVERE BURNS

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THE surgical principles involved in the treatment of burns are often forgotten sometimes ignored in the constant effort to find new and improved methods of treatment. These principles can be expressed very simply by stating the objectives of treatment. They are:

1. To prevent and combat shock.
2. To convert the open contaminated wound into a clean wound.
3. To cover the open wound by the simplest possible dressing that (a) protects it from the constant danger of reinfection (b) does not fix or destroy any part of the skin or subcutaneous tissue which remains viable when the patient is first seen (c) provides for drainage of the serum that exudes from the burned surface until it is checked by pressure or the normal process of coagulation (d) exerts a uniform moderate pressure over the burned area and (e) can be easily removed if infection develops underneath the dressing or if the burn involves the whole thickness of the skin.
4. To keep the injured part at rest.
5. To secure healing in the minimum period of time and with minimum loss of function.

If these principles are sound they apply whatever the extent, the location or the severity of the burn and the effort to classify burns into first, second and third degree or to distinguish between the treatment of burns of the trunk and burns of the face and extremities may only divert attention from essential factors in the treatment.

So much controversy has arisen and so many conflicting ideas have been expressed concerning the local treatment of burns that we wish to postpone for the moment the discussion of the problem of shock and consider first the principles involved in the local care of the burned area.

CONVERSION OF THE OPEN CONTAMINATED WOUND INTO A CLEAN WOUND

This principle often completely ignored in discussions of burns is of primary importance. To cover a burned area with chemical or coagulating solutions without first using every effort to transform it into a clean wound seems to us an inexcusable disregard of fundamental surgical principles.

If the burned patient is still clothed, adherent and burned clothing is best soaked off in a tub of clean water maintained at a temperature of 100 degrees F. in a room reserved and equipped for the treatment of burned patients. The process is rendered almost painless by giving the patient an adequate dose of morphine immediately after admission. We have not used other analgesics or anesthetics even in children with very extensive burns. The room is kept at a temperature of 80 degrees F. and opening of the doors while treatment is in progress is avoided to prevent currents of air from blowing through the room.

With the burned area free from clothing and debris that can be removed by soaking and the surrounding uninvolved area cleansed with soap and water the patient is lifted upon a table covered with a sterile sheet and cleansing of the burned area begun.

To transform an extensive and contaminated raw surface into a surgically clean wound, and without adding further injury and bacterial contamination requires time, patience, gentleness, plenty of soap suds, and continuous irrigation with sterile water of a temperature of 100 degrees F. Obviously the surgeon, his assistants and the patient must be masked. The surgeon and his assistant wear sterile gowns and gloves. Every effort is made to carry out the same careful technique that one would carry out in performing an abdominal operation.

Grease or ointment which may have been applied over the burned surface can usually

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Read before the Chicago Surgical Society, February, 1934.

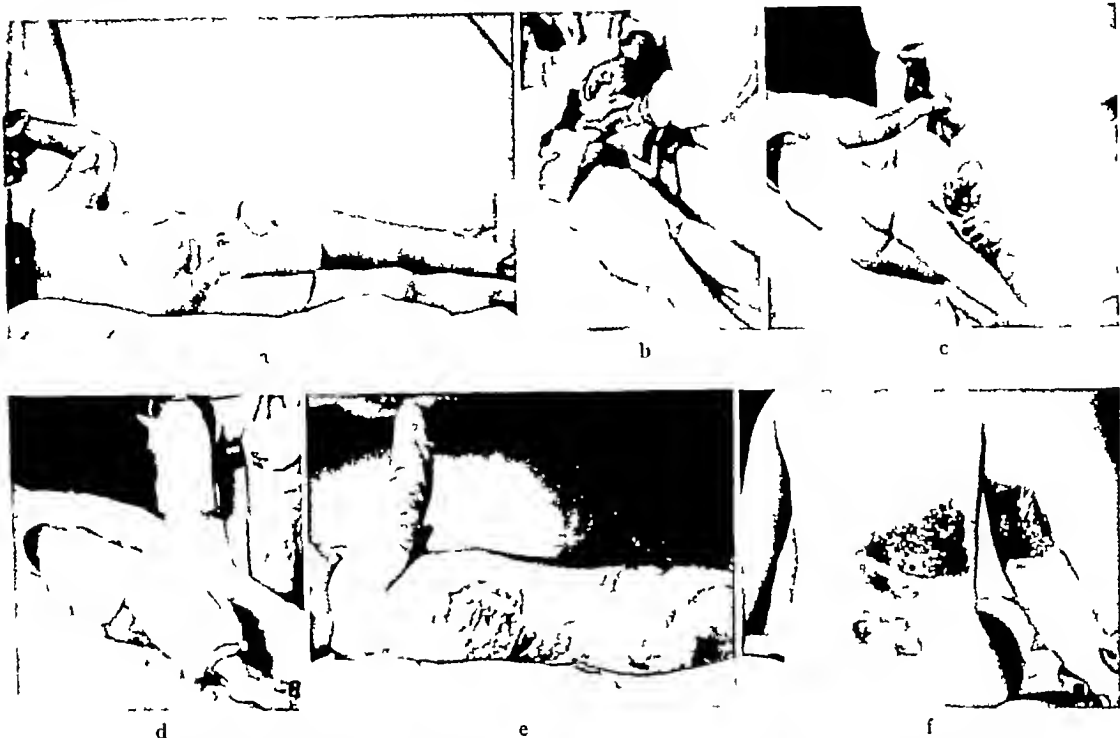


Fig 1 Extensive burn with large areas of whole thickness destruction a, On admission, b, cleansing of burned surfaces, c, excision of necrotic tissue, d, application of

pressure dressing, e, after removal of primary dressing, 13 days after admission, f, appearance of burned areas 20 days after admission, just before application of skin grafts

be washed off with soap suds. If not, a fat solvent such as benzene is used.¹ The actual cleansing is accomplished with large "wash cloths" of soft sterile cotton, plain white soap, and sterile water. Green soap, gauze, scrubbing brushes are avoided as causing unnecessary trauma. Blisters are opened with sterile scissors, shreds of epithelium and skin that can be lifted away with forceps are removed. No excision that might cause bleeding is made.

DRESSING OF THE WOUND

With the injured surface cleansed as completely as possible it is smoothly covered with a few layers of fine meshed gauze impregnated with petrolatum. Such gauze is easily prepared in strips 3 inches wide and 12 inches long and sterilized in a porcelain basin provided with a well fitting cover. This dressing does not adhere to the raw surface as does a

¹Johnston of Detroit has found lard an excellent medium for removing oil and grease. Any lard remaining on the skin can be washed away with soap and water.

coagulant crust, it does not fix tissue, and it still permits drainage of serum and exudate into the dressings outside it.

Over the petrolatum gauze are laid a half dozen layers of flat dry sterile gauze, over this a mass of gauze fluff and over the fluff mechanics' waste or sea sponges so as to provide under the retaining bandage a resilient covering that produces an even pressure over the injured extremity or the burned surface but does not cause constriction.

The dressing and compressing sponges are held in place preferably with an elastic bandage such as stockinet. This is particularly advantageous if the burn involves the trunk.

The advantages of pressure over an injured surface have been well stated by Blair:

"The application of most any dressing produces pressure, but he who employs this pressure in a selective, purposeful manner will get bigger returns than he who applies it incidentally or even as a matter of routine.

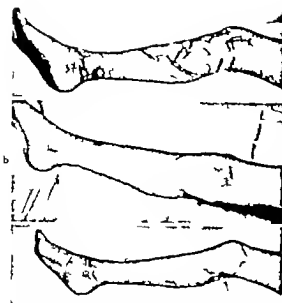


Fig. 2. Extensive burn with loss of partial thickness of skin. a, On admission. b, after seps and water dressing and excision of dermalized tissue. c, on discharge from hospital, 4 days after admission. Burned area healed.

There are chiefly four basic things to be gained by the use of properly applied mechanical pressure to wounds:

The elimination of dead spaces.

The control of oozing.

The limitation of venous and lymph stasis.

Limitation of the amount of plastic material that pours into the wound.

The elimination of dead spaces into which constant oozing can take place and the limitation of exudation from the surface of a wound and into the subcutaneous tissues are

important objectives in wound treatment which are too often completely ignored. The surgeon who sees blood escaping rapidly from an open wound instinctively applies pressure to stop the bleeding and conserve vital body fluid. By some curious inconsistency if we cannot see it we may ignore the subcutaneous bleeding that goes on just as definitely after the subcutaneous rupture of blood vessels and continues until it is arrested either by coagulation or by actual compression of the injured blood vessels by the tensed body tissues.

If this subcutaneous bleeding is the "white hemorrhage" that goes on in tissues injured by a flame or scalding water, it needs to be arrested just as promptly as if the blood were escaping from a torn blood vessel. It can be arrested and body fluid saved by the application of pressure over the injured area.

REST FOR THE INJURED PART

The importance of rest for injured tissues has been emphasized with increasing frequency since war and its accompanying disasters have again focused attention on the treatment of severe and multiple compound injuries. The magic of the plaster cast has proved to be due in large part to the uninterrupted and enforced rest of injured tissues which was so important a principle in the creed of Hugh Owen Thomas. It is as important and essential a part in the treatment of severe burns and of other soft tissue injuries as it is in the care of compound fractures.



Fig. 3. Extensive burn with limited areas of total thickness loss. a, On admission. b, after removal of primary dressing, 4 days later. c, on discharge from hospital, 60 days after admission. Healing of areas of total thickness loss could have been hastened by early skin grafting.

Healing of areas of total thickness loss could have been hastened by early skin grafting.



Fig 4. Severe burn with extensive destruction of covering tissues a, On admission, b, after removal of primary

dressing, c, 13 days later, d, appearance 33 days after admission, shortly before skin grafts were applied

HEALING OF THE BURNED SURFACE

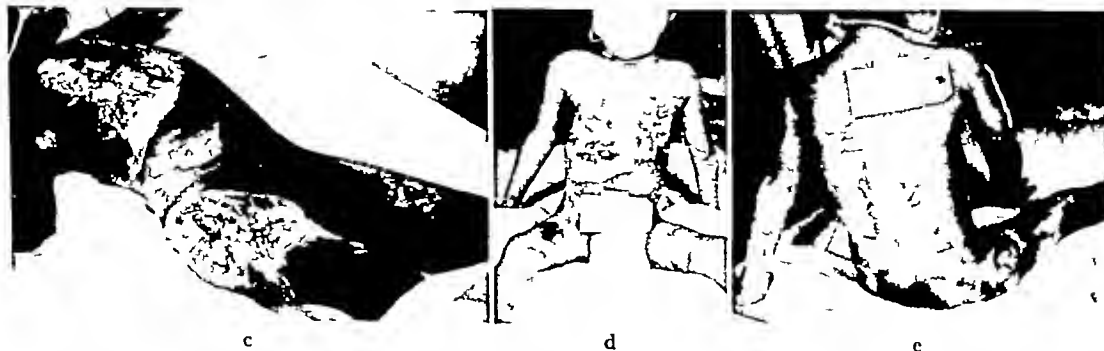
The mechanism of healing after partial or complete destruction of covering skin is sometimes forgotten in the face of the constant emphasis on new methods of treatment which are stressed so strongly by lay writers in *Hygeia*, the *Reader's Digest*, and other nonscientific journals

If there has been loss of only a partial thickness of the skin, in other words, if there still remain epithelial elements—sweat glands and hair follicles—of the deeper portion of the corium rapid re-formation of the covering epithelium takes place (1) if the remaining epithelial elements are not fixed and rendered inert by a coagulating agent, (2) if no infec-



a

b



c

d

e

Fig 5 Severe burn with extensive area of whole thickness loss a, After application of pressure dressing and immobilization with splints b after removal of primary dressing, 12 days later, c, appearance 23 days after ad

mission, d appearance on discharge, 53 days after admission, e, appearance on discharge showing some of grafted areas and on dorsum of trunk, healing of areas from which grafts were taken



Fig. 6a.

tion supervenes. (3) If regenerating epithelium is not torn away and destroyed by careless or frequent or too early removal of the protective dressing.

In cases with loss of partial thickness complete regeneration of epithelium takes place in 10, 12, or 14 days and healing of the burned area should be complete when the primary dressing is first removed at the end of 12 or 14 days.

If the burn has resulted in a whole thickness loss of skin no dressing can bring about regeneration of epithelium. Reformation of covering skin can come only by ingrowth from the periphery or as a result of skin grafting. To await spontaneous healing if the denuded surface is more than 2 or 3 square inches in area is only to delay recovery. Moreover, to wait indefinitely for spontaneous separation of a coagulant crust or of the



Fig. 6b.

Fig. 6. Severe burn involving 44 per cent of body surface. This patient received 8 plasma transfusions of 500 cc. each during the first week, and blood transfusions of 500 cc. each during the second week. a, Patient on fifth day under typhoid tent, fifth burned area covered with compression dressing. Plasma being given through vein in leg; b, c, after removal of primary dressing on fifteenth day; d, just before application of skin grafts on thirty-sixth day after admission. As surfaces are being dressed fifth moist fine-meshed gauze, over which pressure dressing is maintained 7-12 days after admission, 6 days after application of skin grafts; e, 5 days later 57 days after admission.

charred adherent tissue that represents the destroyed surface covering causes serious and unnecessary delay in healing. Cleanly surgical care after the removal of the primary dressing, subsequent dressings at regular intervals of 24 or 48 hours with removal of any adherent tissue that can be cut away without causing pain or bleeding and the use of dressings saturated with Dakin's solution all help to hasten separation of the covering tissue destroyed by the original injury and help to counteract the infection that tends to develop in the presence of an open wound and necrotic tissue.

During this stage of treatment our primary objective is to secure a covering of healthy granulations as soon as possible so that skin grafts can be laid over the raw surface. Here again a number of details in treatment are of great importance. They are (1) cleanly



Fig. 6c.



Fig 6d



Fig 6e



Fig 6f



Fig 6g

(Legend on opposite page)

surgical care, (2) avoidance of trauma, (3) the application of at least one layer of very fine meshed gauze directly over the raw surface so that granulations cannot readily become enmeshed in the gauze, (4) over the fine

meshed gauze moist sterile gauze to favor drainage, (5) over the moist gauze sufficient sterile dry gauze to prevent contamination from without, and (6) the use of pressure to aid the return circulation and prevent the



Fig. 6a.

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Fig. 6c.

what the effect of that loss is on blood volume, blood concentration and blood pressure (1, 3, 8) little emphasis has been laid on the importance of arresting the "white hemorrhage" and preventing the shock producing loss of body fluid

It is to prevent this loss that we have emphasized the importance of pressure applied over the entire burned area or around the affected limb as soon as the open contaminated wound has been converted into a clean wound, and, after the application of the pressure dressing, as complete immobilization of the injured area as it is possible to secure

In spite of every effort to prevent loss of body fluids in patients seen late and in those with extensive burns the loss may be sufficiently great to lead to shock and collapse. In such cases prompt replacement constitutes a life saving procedure. Many workers have made helpful contributions to the solution of this problem, and without discussing in detail the studies of Harkins, McClure, and their associates, of Scudder, of Trusler and his associates, of Rhoads, Wolff and Lee we would simply say that we agree with the statement that "plasma transfusion is the most logical type of replacement therapy and that it has given the best clinical results" (14)

To estimate the extent of fluid loss and the need for replacement during the early and critical stage of treatment the hematocrit reading is an easily obtained and dependable guide. The determination made immediately after admission of a patient with a severe burn can be used as a standard against which to check subsequent readings. Significant changes in blood volume may not be reflected immediately in the clinical symptoms, but a slow steady increase in the hematocrit level indicates that hemoconcentration is taking place and that the loss into the tissues should be compensated for by administration of plasma.

In cases seen late thirst, restlessness, and a rapid pulse rate are constant and important signs of fluid loss and indicate the need for prompt administration of plasma in adequate amounts. To give transfusions of whole blood in such cases, as has been frequently pointed out, may add to hemoglobin con-

centration, and to give water alone in large amounts, as Trusler and his associates have emphasized, may lead to "water intoxication"

The administration of oxygen, particularly in patients with burns of the face and chest, is a valuable adjunct to treatment. In patients with burns of the face and chest the inhalation of irritating gases and the resulting congestion and inflammation of the upper respiratory passages may add another handicap and contribute to the development of anoxemia. We have given oxygen as part of the routine treatment in patients with burns about the face and chest and have thought it to be of definite benefit.

Toxemia The formation of a burn toxin as the result of destruction of the superficial body tissues has been considered by many workers to be the determining factor in causing death in patients with severe burns. Wilson and Stewart and their associates at the Edinburgh Royal Infirmary, particularly, have stressed the frequency with which the picture of acute toxemia develops in from 6 to 50 hours after injury in those cases which go on to a fatal termination. They have emphasized the frequent occurrence of jaundice in these cases and the degeneration and necrosis of the liver seen after death. They have injected into healthy animals "edema fluid" from the subcutaneous tissues of burned animals with resulting fatal toxemia and pathological changes similar to those seen after death from severe burns.

We have no definite evidence either to support or refute the theory that a burn toxin results from destruction of superficial body tissues. The few cases we have observed after death have shown acute degenerative changes in all the parenchymatous organs. The pathological change has not been limited to the liver, nor have we seen the extensive liver changes described by Wilson and his associates.

We would like to point out again that the fatal cases cited by Wilson all received a general anesthetic shortly after the injury. To give ether to a patient with impending shock, particularly a child, seems to us a dangerous procedure, which may well predispose to intensification of shock, the hemocon-



Fig. 7. Extensive burned area coagulated with tannic acid applied by members of Fire Department. Severe infection developed under the crusts, and to remove crusts and necrotic tissue, control infection, and secure healing required 6 months' time. *a*, On admission. *b*, Appearance 4 days after application of skin grafts over large raw surfaces.

congestion that results from the temporary loss of the normal outer retaining wall against which the venous channels can be compressed.

As soon as a covering of healthy granulations is secured and the patient's condition permits, the raw surface should be covered as completely as possible with grafts of intermediate thickness. The sooner this can be accomplished the sooner will recovery be achieved and the less will be the disability and the contracture that steadily increase as long as a raw surface remains unhealed.

COMPLICATIONS FOLLOWING BURNS

The complications resulting from burns have aroused almost as much controversy as the question of local treatment. Many papers have been written on the problem of burn shock, toxemia and infection. Without wishing to oversimplify the problem we would simply state our belief that the initial shock is due to pain, fright, and overexertion and is often followed very quickly by secondary shock resulting from loss and shifting of body fluids; that unequivocal evidence has not yet been produced to show that acute toxemia results from the effect of a circulating toxin formed by autolysis of the burned tissue (Wilson); thirdly, that in the cases under our observation infection developing after a burn has been a feared and serious complication only in patients who were admitted to the

hospital 24 or 48 hours after the injury and whose primary treatment often consisted of the application of ointments of some type.

Shock. Most observers are agreed that primary shock can be severe and is not necessarily dependent on the extent of the burned area. Fright, frantic efforts to avoid injury or to escape from a burning building or from underneath crushing wreckage, sudden and powerful muscular exertion far beyond that normally employed—all can lead to sudden collapse that may appear unexplainable to the observer who sees only an injury of limited extent and severity. For this primary shock morphine is the most effective aid, and in our judgment the morphine need not be supplemented by a general anesthetic. It is of significance to us that the workers who have stressed the theory that a burn toxin is responsible for early death in fatal cases have persistently used anesthetics, including ether, during the initial process of cleansing and tanning.

Many observers are agreed that secondary shock is due to loss of body fluid from the burned surface and still more important *loss of fluid into the subcutaneous tissues*. The latter is comparable to the bleeding that occurs into a crushed limb and although a great deal of effort has been expended to determine how rapidly the loss can take place, how large a percentage of the available body fluid can escape into the subcutaneous tissues, and

MORTALITY RECORD

	Method of treatment	No of cases	No of deaths	Percentage of mortality
1934-1936	Tannic acid	395	39	10
1937 (10 mos)	Tannic acid and silver nitrate (Hedin)	82	6	7.3
1939	Nonadherent dressing with pressure	137	8	5.8
1940		164	6	3.65
1941		185	5	2.7

If we can accomplish these objectives and others of equal importance by a simpler method than the application of tannic acid it means that we are making progress, and not clinging to an outmoded method—even though that method represented a definite advance fifteen years ago.

Under a régime such as that outlined above the results obtained in patients with severe burns in the Children's Surgical Ward of the Cook County Hospital have steadily improved. The accompanying table indicates the mortality record only.

As evidence of the severity of the injuries treated is the fact that of the 19 patients who died as a result of burns in the years 1939-1941, 10 died during the first 24 hours, and 3 during the second 24 hours after admission. Of 6 patients who died later, 3 were transferred from other hospitals, and in these cases the control of infection was an outstanding problem.

In addition to the cases of severe burns were many patients who were not admitted to the hospital or remained in the hospital less than 24 hours. These patients were treated by the same method, and in this group of cases there were no deaths.

Other workers have obtained equally satisfactory results with the method of treatment described. Siler of Cincinnati showed a colored motion picture at Boston in November, 1941, which graphically illustrated the essential details of treatment—wound cleansing, the application of a nonadherent dressing, compression and continued rest, and which showed the excellent results obtained by the application of these principles to the treatment of burns at the Cincinnati General Hospital.

Space does not permit extended discussion of the improved results that have followed

as far as time expended for nursing care, time required to prepare the raw surfaces for skin grafting, and duration of hospital stay are concerned. Nor can one dismiss the subject without emphasizing the constant co-operation on the part of the nursing and resident staff that is essential for good results. The entire nursing staff of the Children's Surgical Ward, the surgical residents,—Lt Clayton Brock now at Camp Shelby, Mississippi, Lt William Requarth, now with Submarine Squadron 4 at Pearl Harbor, and Drs Frederick Leese and W A Yemm of the present resident staff—have all given their constant, whole hearted co-operation to secure the best possible treatment for these seriously injured patients. Without their help it would have been quite impossible to secure the results that have been obtained.

A final word should be added concerning the management of burned patients under emergency conditions. Some of you will say that one cannot possibly carry out the treatment suggested under war conditions or when numerous casualties confront the surgeon.

It is our belief that under such conditions, as well as with patients who come to the surgeon late, or who have received prolonged "first aid" treatment under unfavorable conditions, the sulfonamides can be used to great advantage. An ointment containing a sulfonamide, for example, such as has been successfully used by Allen, Owens, and Dragstedt, can be rapidly spread over the burned surface, covered with a sterile dressing and a compression bandage. The ointment should be applied with a clean spatula and by a masked orderly or nurse. In other words, even under emergency conditions there can be no excuse for not protecting the open wound from contamination with organisms from uncovered mouths and noses.

Patients so treated could be transported to field hospital or casualty clearing station where the treatment outlined in the preceding pages would be carried out. It might well be emphasized again that after cleansing is completed and a pressure dressing applied the patient is left undisturbed for from 10 to 14 days unless some complication arises. If transportation of the patient becomes neces-

centration stressed by Underhill, and the resulting anoxemia which has been stressed by McClure and others as a grave threat to the injured patient.

Infection. For years past infection has hung over the head of the burned patient like a veritable sword of Damocles, threatening life and destroying tissue. No one who has had the responsibility of caring for severely burned patients can erase from his mind the picture of the anxious feverish child with an extensive severely infected raw surface anticipating with constant dread the daily ordeal of change of dressings.

The doctor who asked "Is it true that every patient with an extensive burn eventually develops a blood stream infection?" was simply voicing what has been more or less generally accepted as the inevitable accompaniment of an extensive burn.

To some the statement that infection is the result of careless or unthinking treatment may sound as heretical as Holmes' indictment of the medical profession concerning the responsibility for puerperal infection. Holmes did not know what has since been demonstrated that of almost equal importance with infected hands and contaminated clothing as sources of contagion are the mouth and nose of carriers of virulent streptococci and staphylococci. Here's admirable studies have brought laboratory explanation of the often repeated clinical observation that in most instances the greatest menace to the patient is not the object that causes the open wound, not infection that may have been present on the patient's clothing or on his skin but infection that comes from the open mouth and uncovered nose of excited and voluble bystanders, of enthusiastic first aid workers, too often of the doctor and nurse who are caring for the patient without masking themselves and without making certain that their hands and their surgical instruments are free from pathogenic bacteria.

When we recall the fact so forcefully stressed in a recent editorial by Mason that a burn is in all its essentials a large open wound and when we consider the elaborate precautions every surgeon constantly takes in the operating room to prevent infection of even a small

open wound we cannot but wonder at the inconsistency of failing to take the same precautions in preventing infection of a wound far more extensive than the largest wounds which the surgeon ordinarily sees in the operating room.

If one were to ask the junior medical student why the surgeon and everyone else in the operating room is carefully capped and masked he would have a ready answer. If we were to ask him why in the initial treatment of a patient with an extensive burn, or during the change of dressings in the days following injury such precautions are seldom taken what would he say?

To express it as concisely as possible it is our belief (1) that the most important source of infection of a burned surface is from the open mouth and uncovered nose of individuals working over the injured patient (2) that infection can be prevented in almost every case if the patient is seen promptly after injury and if he has not received extensive or prolonged "first aid" treatment (3) that the simplest and safest method of converting an open contaminated wound into a clean wound is by gentle, thorough cleansing with plain white soap and sterile water applied with gloved hands under eyes that are alert and mouth and nose that are carefully masked and (4) that it is neither logical or wise to substitute for a safe and tested method an elaborate time consuming procedure which involves the use of powerful chemicals concerning whose possibilities for harm we are still in doubt.

To say that the application of a coagulant over a burned surface is not the ideal or most desirable type of dressing in no way detracts from Davidson's splendid contribution to the problem of burn treatment. Davidson taught us two important facts that if a burned surface is covered promptly with an occlusive dressing the constant danger of infection of the large open wound is eliminated and secondly that the prompt application of a dressing which checks the constant loss of serum from the burned surface diminishes the loss of vital blood plasma.

*Cases of cellulitis preventing and thereby resulting from the application of ichthammol to the incision as recommended by Pickard, have been reported.

INVERT SUGAR AS A SUBSTITUTE FOR GLUCOSE IN INTRAVENOUS THERAPY

S E KERR, Ph D , Newark, Delaware, and R J PAULY, Ph D , Beirut, Republic of Lebanon

INABILITY to secure glucose because of blockade and interruption of commerce by the war resulted in the trial of invert sugar for intravenous therapy, with satisfactory results. The following report on the method of preparation of invert sugar solutions from ordinary cane sugar and the results observed will be of especial interest wherever hospitals are isolated from their usual sources of supply.

During the last world war (1914-1918) Mayer and Guerbet used invert sugar prepared from sucrose for intravenous injections, because of difficulty in obtaining pure glucose, which at that time was frequently contaminated with lead and arsenic. They stated that the physiological and therapeutic actions of the invert sugar preparation were identical with those of glucose. Even though glucose of satisfactory quality was available soon after the war, the use of invert sugar rather than glucose continued in Germany at least up to 1930 (9). Invert sugar solutions for intravenous use were placed on the market in Germany under the proprietary name of "calorose" (10, 12), and methods for making non-proprietary substitutes for "calorose" were published by Danish pharmacists in 1930 (7). Cousin and Fagon in 1937, finding difficulty in securing pure glucose in the French colonies, turned to the use of invert sugar, using a modified form of the method of Mayer and Guerbet. In the American literature we have found no references to the use of invert sugar for therapeutic purposes.

The earlier methods recommended for the preparation of invert sugar solutions for parenteral use depended upon the hydrolysis of sucrose with phosphoric acid (3) with subsequent removal of phosphate as the calcium salt by interaction with calcium carbonate, or

with tartaric (12) or hydrochloric acid (7), the acids being subsequently neutralized with sodium carbonate. Hansen, Shou, and Tonnensen used small amounts of hydrochloric acid as the hydrolytic agent with no attempt at neutralization, producing solutions with a pH of about 3.

We have adopted a method recommended for the preparation of invert sugar solutions for use in the so called Boeseken titration (1). In this procedure a hot concentrated solution of sucrose is hydrolyzed rapidly with hydrochloric acid, which is then exactly neutralized with an equivalent amount of sodium hydroxide. The resulting solution diluted to a concentration of 5 per cent (calculated as hexose) is a clear, colorless liquid with a pH between 4.5 and 6.0, containing not more than 0.01 per cent of sodium chloride and 0.05 per cent of unhydrolyzed sucrose.

REAGENTS

Freshly distilled water (not over 12 hours old) should be used in the preparation of all reagents, as well as for solution of the invert sugar. It is well known that reactions following intravenous injections of saline or glucose are most frequently due to the use of distilled water in which "pyrogenic" bacteria have grown.

Hydrochloric acid Prepare a solution approximately normal in strength by a 1 to 10 dilution of concentrated (38 per cent) hydrochloric acid.

Sodium hydroxide It is essential that this be of exactly the same normality as the hydrochloric acid. Adjust the concentration of a 5 per cent solution until 25 cubic centimeters of the hydrochloric acid solution are exactly neutralized by the same volume of the sodium hydroxide solution. Keep in a paraffined bottle provided with a siphon and a soda-lime tube to prevent contamination with silica and carbon dioxide.

From the Biochemical Research Foundation, Newark, Delaware and the Departments of Biological Chemistry and Pharmacology, American University of Beirut, Beirut, Republic of Lebanon.

sary it can be accomplished with minimum difficulty and without change or interruption of treatment. In other words, the simplicity of both the initial treatment and the post operative care should commend such a method if it is based on sound surgical principles.

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TABLE I—TOTAL REDUCING SUGAR AND LEVULOSE IN BLOOD DURING AND AFTER INTRAVENOUS INFUSIONS OF INVERT SUGAR*

Subject	Invert sugar injected	Fasting		During infusion			End of infusion			30 min. after end of infusion		60 min. after end of infusion	
		Reducing sugar	Levulose	Inter val†	Reducing sugar	Levulose	Inter val	Reducing sugar	Levulose	Reducing sugar	Levulose	Reducing sugar	Levulose
Bed 11	900 c.c. 5%	72	2				35	150	12.7	83	6.3		
Bed 13	900 c.c. 5%	80	2.2				43	200	15.6				
Bed 15	900 c.c. 5%	72	1.6				49	135	13.1				
SEK	900 c.c. 5%	76	3.0				84	100	11.5	70	6.5	68	5.7
JJ	900 c.c. 5%	74	4.1				61	113	9.9	50	5.3	68	4.2
Ham	900 c.c. 5%	72	2.7				63	117	11.0	52	9.1		
Far	500 c.c. 10%	66	2.8	27	130	15.3	45	117	17.3	46	5.0	60	4.6
St	500 c.c. 10%	78	3.6	19	156	14.5	43	180	18.0	62	6.3	56	4.7

*Results expressed in milligrams of sugar per 100 cubic centimeters of blood.

†Number of minutes after beginning the infusion

sugar was at this time in most cases considerably below the fasting level—a phenomenon also observed when only glucose is injected

The small amount of unhydrolyzed sucrose in the invert sugar solutions is promptly excreted in the urine. Excretion of reducing sugar varies between 0.6 and 1.1 grams during infusion

ADVANTAGES OF LEVULOSE

Since invert sugar is half glucose and half levulose, any question regarding justification for its use must involve the intermediary metabolism of the levulose fraction. The review by Deuel as well as other literature supplies ample evidence that levulose is readily converted to glucose and glycogen in the body. It is easily oxidized and causes a prompt rise in the respiratory quotient and in heat production. There is considerable evidence which suggests that levulose is more readily utilized in diabetes mellitus than glucose.

SUMMARY AND CONCLUSIONS

No unfavorable reactions were observed in 2,349 cases following intravenous injection of

invert sugar prepared by acid hydrolysis of commercial sucrose. The levulose fraction disappears rapidly from the blood stream, 18 milligrams per 100 cubic centimeters being the highest value observed at the end of an infusion. The results confirm the experience of others that when glucose is not available invert sugar is a satisfactory substitute for intravenous therapy.

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Indicator For adjustment of hydrogen ion concentration a convenient indicator is made by mixing equal parts of methyl orange (0.1 per cent in 50 per cent alcohol) and brom-cresol-purple (0.04 per cent in water). This indicator when used in the proportion of 4 drops per 5 cubic centimeters of solution, gives a yellow color between pH 4.4 and 5.8 (a range suitable for intravenous injection). Below pH 4.4 the indicator gives a reddish color and above 7.0 a purplish color.

Hydrogen-ion concentration standards Although the hydrogen ion concentration may be adjusted to within the proper range by merely observing the color given by the indicator as herein noted, it is advantageous to have known standards for reference. Nine standards between pH 4.0 and 7.2 with intervals of 0.4 are sufficient. Directions for the preparation of these may be found in any biochemical manual (e.g. Cole). Measure 5 cubic centimeters of each standard into test tubes and add to each 4 drops of the indicator.

METHOD OF PREPARATION OF INVERT SUGAR SOLUTION

Twenty liters of sterile invert sugar solution may be prepared by the following procedure. Dissolve 960 grams of sucrose (commercial granulated table sugar) in 300 cubic centimeters of freshly distilled water in a 2 liter Erlenmeyer flask with the aid of heat and with continuous rotation of the flask to avoid caramelization then bring to the boiling point and boil for a minute or two until clear. With a pipette add exactly 25 cubic centimeters of normal hydrochloric acid and mix the contents of the flask by rotation for 1 minute. Immediately neutralize while mixing, by adding 300 cubic centimeters of water containing exactly 25 cubic centimeters of the sodium hydroxide solution. The solution should have no more than a light yellow color. The volume is about 1500 cubic centimeters and contains the correct amount of invert sugar to make 20 liters of 5 per cent solution (glucose equivalent).

The stock solution is filtered while still warm through four thicknesses of muslin and then through one thickness of filter paper.

Adjustment of hydrogen-ion concentration Dilute 3 cubic centimeters of the concentrated preparation to 40 cubic centimeters and mix. To 5 cubic centimeters of this diluted solution add 4 drops of the indicator and compare with the pH standards. If the pH is not within the range 4 to 6.8 (a yellow color indicates 4.4-5.8) titrate 15 cubic centimeters of the concentrated sugar solution with 0.01 normal sodium hydroxide (or hydrochloric acid if it is too alkaline) using 12 drops of indicator and end the titration at a pH between 4 and 5. To the main solution (1500 cubic centimeters) add a quantity of normal sodium hydroxide (or hydrochloric acid) equal to this titration and mix. Again dilute 3 cubic centimeters to 40 and test the pH.

The stock solution is finally diluted to 20 liters with freshly distilled water within 48 hours, measured into flasks or ampuls and sterilized by autoclaving at 120 degrees C. for 30 minutes. Each flask is inspected for fiber particles before autoclaving and refiltered if necessary.

RESULTS

In a period of 5 months when glucose was not available (November 21, 1940 to April 18, 1941) 2,349 flasks of invert sugar were used for parenteral therapy in the hospitals of the American University of Beirut. Not a single reaction was observed. Previous to this period (November 1, 1939 to October 31, 1940) three reactions occurred in the treatment of 6,180 cases with glucose solutions.

Determinations of total reducing sugar and of levulose in blood were made during and after intravenous injections of invert sugar in normal subjects. The method of Herbert was used for levulose, and that of Shaffer and Somogyi for total reducing sugar both determinations being carried out on a zinc hydroxide filtrate of the same blood specimen. The results, presented in Table I, show that the rise of blood levulose is much less than that of glucose the maximum value observed for levulose being 18 milligrams per 100 cubic centimeters at the termination of an infusion of 500 cubic centimeters of 10 per cent invert sugar. Half an hour after the end of the infusion, blood levulose varied from 5 to 9 milligrams per 100 cubic centimeters while total reducing

TABLE I — CURE RATES REPORTED FOR CANCER OF THE OVARY

	Total cases	Per cent cure
Schaefer	74	16.2
Stuebler and Brandess	122	24.5
Schleyer	126	9.5
Wintz	87	17.2
Norris and Murphy	93	53.8
Taylor	84	8.3
Schroeder	56	32.1
Heyman	134	32.1
Lynch	62	35.5
Meigs	147	16.0
Pemberton	114	32.0
Walter Bachman and Harris	63 (No x ray) 61 (x ray)	6.3 29.0

than the adenocarcinomas, they nevertheless do frequently metastasize and cause the patient's death. These tumors should, therefore, be included in any series of cases of cancer of the ovary although tables should be so constructed that the part they play in the final figure for the whole series is apparent.

Adenocarcinomas of the ovary In the largest group, the papillary serous and pseudomucinous adenocarcinomas, 88 in number, there was a 5 year cure rate of 15.9 per cent. The cure rate among the 25 pseudomucinous tumors was 5 or 20 per cent, among the 63 serous adenocarcinomas, 9 or 14.3 per cent.

Granulosa cell tumors Of the 16 cases of granulosa cell tumors, 11.6 per cent of the

TABLE II — RESULTS IN RELATION TO EXTENT OF DISEASE

	Total cases	Per cent frequency	Per cent cured
Complete surgical removal	44	31.9	45.5
Partial removal	50	36.2	4.0
Exploration only	29	21.0	0.0
Recurrent cancer	15	10.9	0.0
Total	138	100.0	15.2

series, there were 5 definite 5 year cures and 7 cases in which the patient died or in which metastasis was present when the patient was last observed. The exclusion of the granulosa cell tumors from the entire series would lower the 5 year cure rate to 13.9 per cent, an insignificant change.

Other special tumors The dysgerminoma is represented in this series by 2 patients, both of whom died of their disease shortly after treatment. There were 2 patients with squamous cancer developing in a dermoid cyst, both of whom also died within a few months of their operation. Four cases classified as mesonephroma (Schiller) resulted in 1 cure and 3 deaths from recurrence.

Melastatic tumors There were 4 ovarian carcinomas with endometrial cancer in which there was a doubt as to the primary site of the tumor. In this group there was one 5 year cure. In another patient classified with the granulosa cell tumors, there was an independent primary cancer of the endometrium.

In 12 cases originally classed as cancer of the ovary, histological review suggested that the tumor might have originated in the stomach or large intestine. All of these patients

TABLE III — FREQUENCY AND RESULTS IN INDIVIDUAL TYPES

	Cases	Frequency	Cures	Per cent cured
Papillary serous adenocarcinoma	63	45.6	9	14.3
Pseudomucinous adenocarcinoma	25	18.1	5	20.0
Granulosa cell tumor	16	11.6	5	31.3
Dysgerminoma	2		0	
Mesonephroma	4		1	
Cancer in dermoid cyst	2		0	
Associated endometrial cancer	4		1	
Possible gastrointestinal primary	12		0	
Unclassified	10		1	
Total	138			15.2

TABLE IV — RESULTS IN RELATION TO HISTOLOGICAL GRADE IN ADENOCARCINOMAS

	Total cases	Cures	Per cent cured
Papillary serous adenocarcinoma Grades 2 and 3	45	2	4.4
Pseudomucinous adenocarcinoma Grades 2 and 3	7	0	0
Papillary serous adenocarcinoma Grade 1	18	7	38.8
Pseudomucinous adenocarcinoma Grade 1	18	5	27.7
Total	88	14	15.9

FACTORS INFLUENCING THE END RESULTS IN CARCINOMA OF THE OVARY

Report of a Series of 138 Patients Treated from 1910 to 1935

HOWARD C. TAYLOR, Jr. M.D. F.A.C.S., and ARTHUR V. GREELEY M.D. F.A.C.S.,
New York, New York

REPORTS on the results of the treatment of ovarian cancer have exhibited a range from below 10 to over 50 per cent of 3 to 5 year cures (Table I). This wide variation is evidently the result of other factors beside the relative merits of therapy as applied by the reporting clinics and must almost certainly be ascribed to different methods of classification or the statistical handling of the case material.

The calculation of any 5 year cure rate is carried out principally to make possible the selection of the best of several methods of therapy or to demonstrate the need of some special procedure, such as postoperative radiation. Statistics on malignant ovarian tumors have failed in this purpose because of the heterogeneous character of the group and the differences of opinion as to how it should be reported.

In the present article this problem will be examined in the light of a series of patients treated at the Roosevelt Hospital. At the same time the end results for these cases will be presented and the effects of radiation therapy reported.

For this work 198 cases of ovarian tumor have been reviewed, including 138 cancers of the ovary and 60 papillary cystadenomas. The series includes all cases belonging to these categories, the patients being admitted to the gynecologic service from 1910 to 1935.

The "absolute" 5 year cure rate among the 138 malignant cases has been placed at 15 per cent, when all cases are considered and the lost cases are counted as dead. This figure is approximately that recently reported by Meigs (6) in his review of cases at the Massachusetts General Hospital, but is much lower than the recent figures of Pemberton or of Walter et al.

The principal factors which may vary the actual end-results, as well as the figures as reported, will now be considered. These are four in number: the gross extent of the disease, the histological type of tumor, the histological grade of the tumor, and the use of radiation therapy.

GROSS EXTENT OF DISEASE (TABLE II)

It is well recognized that the gross extent of the ovarian carcinoma at the time the operation is undertaken is the most important single consideration in prognosis. If one defines an operable case as one in which all cancer was apparently removed, the operability of this series was 31.9 per cent. The known cures in this operable group were 45.5 per cent, while if the many cases untraced for the necessary 5 years, but free of disease when last seen, be excluded, the 5 year cure rate in the operable group becomes 58.8 per cent. The other side of the picture is as gloomy as this is encouraging, for of the 94 cases in which malignant tissue was left behind at the conclusion of the operation or which were recurrent, only 2 have survived the 5 year period.

TYPES OF OVARIAN TUMOR (TABLE III)

The cancers of the ovary are distinguished by the diversity of their cells of origin, and evidence has been presented in the literature to show that certain of the special types, such as the granulosa cell tumors and dysgerminomas, have a relatively favorable prognosis. For this reason some writers on this subject have considered it wise to exclude these special tumors from series of cases of ovarian cancer on which 5 year end results are reported. To make this exclusion seems to us to render the record incomplete, for although the special types are probably in general less malignant

Read before meeting of the American Radiology Society at Cleveland, Ohio, June 2, 1941.



Fig 5 Pseudomucinous cystadenoma. Originally diagnosed as malignant. Five year cure (SD2724)

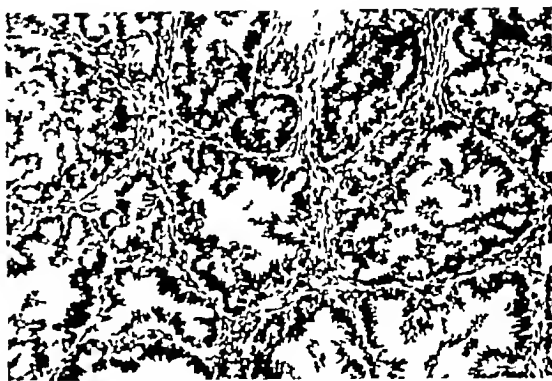


Fig 6 Pseudomucinous cystadenocarcinoma. Malignancy doubtful. Five year cure (SC9376)

In a series of cystadenomas and adenocarcinomas of the ovary, the morphological transition from the benign to the malignant takes place almost imperceptibly. No pathologist has had the experience to place the line of division exactly. The uncertainty of histological diagnosis in this group of tumors is exemplified by 6 cases.

The following papillary serous tumors are only a part of those about which there was disagreement.

C F (No 2,649, Fig 1). An unmarried woman of 35 years was operated upon at the Roosevelt Hospital on July 24, 1913. Bilateral cysts of the ovary with multiple intestinal implants were discovered and, although a complete hysterectomy with removal of both adnexa was performed, neoplastic tissue remained in the abdomen. In spite of these findings the patient was quite well 13½ years after her operation. A pathological diagnosis (B-3,867) of pap-

illary cystadenoma was made, and this diagnosis was confirmed by the patient's course.

H L (No 20,489, Figs 2 and 3). A married woman of 35 years had a right oophorectomy on January 12, 1933, for a small cyst, discovered after operation to be filled with papillary material. On the basis of slides (SD7,852) a diagnosis of "papillary cystfibroadenoma (benign)" was made (Fig 2). Two years later she was operated upon again and found to have a solid tumor in the right side of the pelvis and metastatic nodules in the abdominal wall and omentum. The diagnosis (SD1,949) was now changed to papillary cystadenocarcinoma (Fig 3).

H W (No 13,388, Fig 4). A married woman of 34 years was admitted to the hospital June 19, 1920. At operation an apparently inoperable condition was found and a diagnosis was made of papillary cystadenocarcinoma. The disease did not progress, however, and the uterus and adnexa were successfully removed 18 months later. A histological diagnosis was then made of papillary cystadenoma (SA9,775). She remained well for 3 years after which ascites appeared. Seven years after the beginning of her



Fig 7 Pseudomucinous cystadenocarcinoma. Originally diagnosed as benign. Died in 13 months (C3181)



Fig 8 Papillary serous cystadenoma. Benign type. Ten year cure (SB6723)



Fig. 1. Papillary serous cystadenoma. Clinically diagnosed as malignant. Ten year cure (B-3567)



Fig. 2. Papillary serous cystadenocarcinoma. Originally diagnosed as benign. Recurrence in 7 years (SC7831)

are dead. The exclusion of these 13 cases would raise the original 5 year cure rate to 17.4 per cent.

Unclassified cases The histological material was either lacking or unsatisfactory in 10 cases among which there was 1 cure.

It is noteworthy that the exclusion of any of these rather small groups has very little effect on the 5 year cure rate of 15.2 per cent that has been noted for the series as a whole

HISTOLOGICAL DEGREE OF MALIGNANCY (TABLE IV)

Although it has been repeatedly stated that 'grading' has no bearing on the results of treatment in ovarian cancer most reports indicate that there is a relatively favorable outlook for the more differentiated papillary adenocarcinomas of the ovary (Pemberton

Lynch, Meigs, 6) Other writers, who speak of malignant degeneration in papillary cystadenomas are apparently referring to the same group (Stuebler and Brandess). Still other writers use the term papillary cystadenoma for tumors that have from the clinical standpoint a malignant course (Moench). It seems best to us to designate these differentiated types, which are capable at times of recurring and killing the patient, as grade 1 adenocarcinoma of the ovary.

If the recognition and segregation of this type may be termed "grading" then the grade of malignancy in ovarian cancer is of enormous prognostic significance. The classification of 88 cases of ovarian adenocarcinoma, Table IV indicates only 2 cures, among 52 undifferentiated types whereas among 36 so called grade 1 cases there were 12 cures.

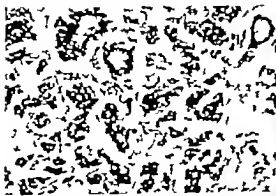


Fig. 3. Infiltrating carcinoma in recurrence from tumor of Figure 1 (SD7049)

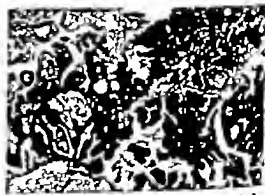


Fig. 4. Papillary serous cystadenocarcinoma. Originally diagnosed as benign. Died after 7 years (S 4771)



Fig 5 Pseudomucinous cystadenoma Originally diagnosed as malignant Five year cure (SD2724)



Fig 6 Pseudomucinous cystadenocarcinoma Malignancy doubtful Five year cure (SC9376)

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Fig 7 Pseudomucinous cystadenocarcinoma Originally diagnosed as benign Died in 13 months (C3181)



Fig 8 Papillary serous cystadenoma Benign type Ten year cure (SB6723)



Fig. 9. Papillary serous cystadenofibroma. Benign type (SE266)

disease an exploratory operation was performed again and in spite of an identical histological structure, the diagnosis was changed back to papillary cystadenocarcinoma. Ten years after the onset of her disease she died.

The pseudomucinous tumors offer similar problems, as can be seen from the following 3 cases.

31 R (No C 35463, Fig. 5) A single woman of 5 years was operated upon on December 6, 1935. A large cystic tumor was found and a right salpingo-oophorectomy was performed. An original diagnosis of carcinoma (S.D. 724) was made but this opinion was reversed after outside consultation and the case is now carried in our records as benign. She is free of recurrence after 5 years.

C.C. (N 54, Fig. 6) A married woman of 3 years was operated upon in the fourth month of her pregnancy and a right salpingo-oophorectomy was undertaken. The patient as delivered of normal child at term and has since remained well. Slides (S.C. 9376) are submitted for pathological examination independently. T regarded the condition as benign and two as malignant. On account of the recognized authority of pathologist who called this cancer the case has been carried in our carcinoma series although it is our belief that almost all tumors of this type will be cured.

31 P (No 563, Fig. 7) A married woman of 60 years was operated upon on November 2, 1935 and a large multilocular cyst of the right ovary was found. The operation consisted in complete hysterectomy and bilateral salpingo-oophorectomy. Metastasis was present and diagnosis of papillary cystadenoma was made (C3 8). Nevertheless, the tumor rapidly recurred, causing the patient's death in 3 months. The diagnosis was accordingly changed to adenocarcinoma.

There are then 2 possible changes in our histological classification of cases which would



Fig. 10. Pseudomucinous cystadenoma. Benign type (SD5546)

fundamentally affect our own reported cure rates. (a) Certain of the cases classed as papillary adenocarcinoma might have been benign. Actually 12 of the 14 cured cases of adenocarcinoma were regarded as well differentiated and classed as grade 1. (b) On the other hand some of the 60 papillary cystadenomas were perhaps malignant. There are no known recurrences in this group. Nevertheless, 4 were noted to have had peritoneal implants at the time of their operation and 6 were labelled carcinoma by the first pathologist. In all at least 26 of the 60 papillary cystadenomas were somewhat doubtful (Table V).

It is interesting to note what an effect changes in the classification of these two categories, those here regarded as grade 1 adenocarcinomas and a doubtfully benign or actively proliferating papillary cystadenomas, would have on the reportable cure rates of the Roosevelt Hospital cases. The exclusion of 12 cured grade 1 cases would have reduced our 5 year rate in the cystadenocarcinoma group

TABLE V.—HISTOLOGY OF PAPILLARY CYSTADENOMAS OF OVARY 1910-1935

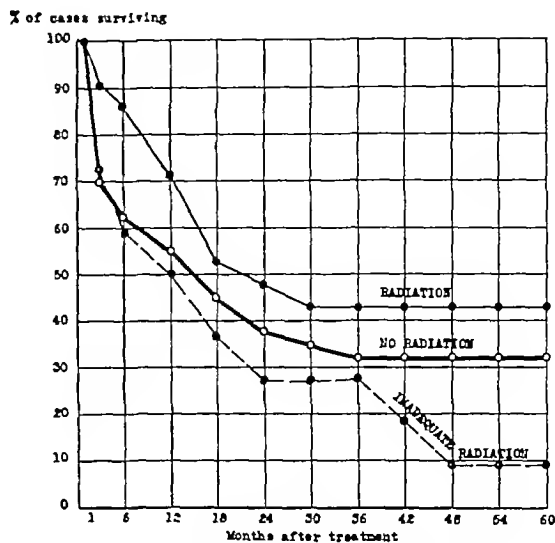
	No. cases
Serous cysts of borderline histology (Fig. 8)	8
Serous cysts with active epithelial proliferation (Fig. 8)	14
Serous cysts with papillary fibroadenomas (Fig. 9)	5
Pseudomucinous cysts of borderline histology (Fig. 5)	4
Benign pseudomucinous cysts (Fig. 10)	4
Inadequate tissue for classification	60
Total	95

to 2.6 per cent, in the entire series of ovarian cancer to 7.9 per cent. On the other hand, if the 26 "borderline" cystadenomas had been added to the cures, the 5 year cure rate of the adenocarcinomas would have been 35 per cent, the cure rate for the entire series, 29.2 per cent. A range of 8 to 35 per cent of 5 year cures in ovarian "cancer" is about what may be found in the literature.

Difference of opinion as to what histological features justify the classification of some of these borderline tumors as benign or malignant, is probably the most important variable governing the reported figures on cures of ovarian cancer. A slight change in conception of the morphological criteria of malignancy in the cystic tumors of the ovary appears to us largely to explain the change in our own figures from the 8.3 cure rate of our 1934 report to the 15.2 per cent noted in the present article.

RADIATION THERAPY

Postoperative x-ray treatment of ovarian cancer was begun at the Roosevelt Hospital in 1928. For the first 3 years the therapy consisted as a rule, in a single high voltage treatment given to each of four fields, but insufficient in amount to produce a skin erythema. From 1931 to 1933 the commonest plan of therapy was based upon four pelvic fields, each receiving 670 r in one dose, the factors being 200 kilovolts, 50 centimeters target-skin distance, 1 millimeter aluminum and 0.5 millimeter of copper filtration, 5 milliamperes of current, for 70 minutes, with fields of 20 by 20 centimeters. From 1933 to the present various plans to give divided dosage have been employed, the commonest being the use of four fields, each receiving five exposures of 300 to 360 r at each treatment. The factors employed for delivery of these treatments were usually 200 kilovolts, 50 centimeters distance, 2 millimeters of aluminum and 0.75 millimeter of copper filtration, 25 milliamperes of current, for 9 minutes with fields of 15 by 15 centimeters. In the tabulation of these cases, those which received 650 r or more per port in a single treatment or a series of small treatments totaling 1500 r or more have been classed as receiving "ade-



Graph 1 Effect of x-ray therapy on survival in cases of ovarian cancer

quate" radiation and are to be distinguished from those receiving incomplete x-ray courses or small doses of radium in the uterus or vaginal vault.

Among the 82 patients receiving no radiation there were 5 year cures in 12, 14.8 per cent, among the 26 patients receiving "adequate" radiation therapy, there were 5 year cures in 9, 34.6 per cent, and among the 30 patients receiving incomplete radiation there was 5 year cure in only 1, 3.3 per cent. It is noteworthy that all but 2 of the radiation cures are in the relatively differentiated type in which cure frequently results simply from surgery. In 2 cases alone, those in which some carcinoma remained after the conclusion of the operation, x-ray appears to have been the essential factor in producing a cure.

A better method perhaps of studying the effects of x-ray is in the construction of a curve for survival rate (Graph 1). The curve is based on 82 cases, in which patients survived their operation by at least 1 month and in which the exact month of patient's death because of cancer is known. The curve of survival for the patients receiving "adequate" x-ray is consistently higher than the basic curve for the nonradiated cases but is of essentially the same shape. It should be

noted further that had the deaths within the first 3 months been eliminated the two curves would have been almost exactly superimposed. The very low survival curve of the cases receiving "inadequate" radiation is probably an example of the range of variation which may be expected in building curves on small samples of cases, but might be due to the fact that it includes a number of patients who were too sick to complete their treatment. It does not appear to us that radiation, as given at the Roosevelt Hospital, has materially affected the average duration of life in cases of ovarian cancer.

Strikingly beneficial effects from x-ray therapy in ovarian cancer have been reported from many sources (Harris and Payne, Heyman, Montgomery and Farrell, Schins and Zuppinger, Schroeder, Wintz, and Walter Bachman and Harris). Yet the best cure rates reported after postoperative x-ray therapy still lie within the limits of the best figures reported for cases not treated by radiation. Furthermore few if any reports based on contrasted series treated in the same institution have eliminated the possibility of the favorable selection of patients assigned to radiation. It does seem probable to us that in an occasional case as cited in this series, the x-ray is the essential factor in producing a 5 year cure but it appears unlikely that postoperative x-ray can be expected to transform a cure rate of 6.3 per cent to 29.0 per cent as indicated in the recent paper of Walter Bachman and Harris.

SUMMARY AND CONCLUSIONS

1. The reporting of statistics on ovarian carcinoma, on account of the heterogeneous character of the disease requires the listing of special types with their individual end results as well as figures for the whole. The special types, such as granulosa cell tumors and dysgerminomas, should be placed in special categories. The adenocarcinomas should be graded and at least those capable of different interpretation by different pathologists considered as a group. In this respect it is necessary to include a note on the papillary cystadenomas treated in the hospital during the same period since if this group is very

small it is probable that some have been erroneously classed with the cancer cases. Tumors possibly primary outside of the ovary should not be disregarded simply because the primary ovarian character cannot be absolutely established.

2. In the present series of 138 cases of ovarian cancer the absolute 5 year cure rate is reported as 15.2 per cent. The factor which most affected prognosis was the gross stage of the disease at the time of operation. Of next importance was the histological grade of the tumor at least in the sense that the differentiated tumors of perhaps doubtful malignancy had a very much better prognosis than the others.

3. Postoperative x-ray therapy was apparently responsible for the 5 year cure of 2 cases, in which recurrence was otherwise certain but the effect of x-ray on the percentage of 5 year cures and on survival curves was less than has been frequently claimed.

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FRACTURES OF THE FOREARM

Some Technical Procedures

ARTHUR L. MURPHY, M.D., F.A.C.S., Halifax, Nova Scotia

REDUCTION, retention, and restoration of function are the basic principles of fracture therapy. The techniques developed from these broad themes are legion. In their little details lies ultimate success or failure. Perhaps in no other branch of surgery do trifles loom as great. Our methods of dealing with two common forearm fractures do not infringe on basic principles; they have helped with trifles.

In the ubiquitous Colles' fracture, the great postreduction problem is circulatory obstruction. Originally I splinted these fractures with circular plaster, attempting to make the cast thin enough that, when split on the ulnar side, it would yield to the swelling wrist. Good in theory, the figure of eight windings around wrist and hand made an unavoidably rigid plaster. Forcing its cut edges apart was difficult and sometimes resulted in a loss of the reduction. The simple dorsal or ventral plaster mold did not give the desired stability. Hence, the spiral mold.

The mold (Figs. 1, 2, 3) is made of one to two 3 inch by 3 yard bandages. The crinoline-impregnated type is most satisfactory, giving greater strength per ounce. The mold is rolled dry, the distal end is cut obliquely to make a narrow strip across the palm. It is dipped in water, and applied without padding—this is essential. Beginning on the palm, embracing the hypothenar eminence, its distal edge follows the proximal crease of the palm till it passes between thumb and index finger. The angulated edge (made by cutting the end of the mold) is radial, and ends just distal to the radial styloid, so that the full width of the plaster covers the site of the fracture. The mold is continued around the arm to end just distal to the medial epicondyle of the humerus.

The mold is held in place by a wet gauze bandage, the palmar strip being shaped well to fit the palmar arch.

In most cases swelling of the hand will be so slight as to demand no interference. The patient may be sent home without fear of an ischemia developing over night. If swelling does become troublesome it must be relieved. The gauze bandage is cut along the lateral border of the hypothenar eminence, the plaster and injured wrist are supported firmly on their dorsum, the palmar strip of plaster is levered free from its hypothenar end, and then restrapless less tightly. The fracture area has not been disturbed.

After 10 to 14 days the spiral mold is replaced by a simple dorsal mold with the hand in dorsiflexion.

It may be observed in Figures 2 and 3 that the hand is not in the position of flexion too often shown as the correct one for holding a Colles' fracture in reduction. Originally described by Cotton, the technique of reduction has grown to a beautiful example of surgical mechanics. The first movement is pronation. Through the leverage of the hand and carpal ligaments this forces the distal, radial fragment downward, ventrally. The second movement of ulnar deviation, by traction on the radial-carpal ligaments, opens the

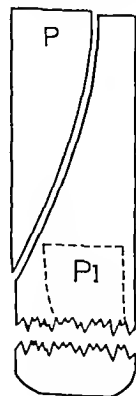


Fig. 1. Fragment *P* serves to reinforce the mold over the wrist joint at *P*₁.

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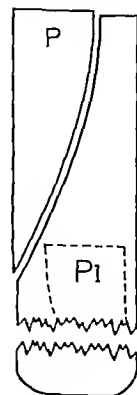


Fig 1. Fragment P serves to reinforce the mold over the wrist joint at P₁.



Fig. 2.

Fig. 3.

Fig. 4.

Fig. 5.

Figs. 2, 3, 4, 5 are posed by interneos, as the mold has been applied to the fractured arm must be bandaged on. Ob-

viously the Kirschner wire in Figure 5 does not pierce the phalanx.

space into which it descends. It also corrects the lateral displacement. The third movement flexion, in this position is limited to about 25 degrees. It simply locks the distal fragment in place and helps to correct the dorsal tilt of its articulating surface.

The spiral mold was devised originally to overcome a problem met in treating fractures of the phalanges and metacarpals particularly Bennett's fracture at the base of the first metacarpal. Abduction of the thumb rarely gives a satisfactory reduction without traction. In using a wire, projecting from a plaster arm cuff to take the traction through an elastic band to the Kirschner wire in the proximal phalanx, we found that the cuff (pushed tight by countertraction) often

caused circulatory obstruction in the arm. The spiral mold (Figs. 4 and 5) bandaged with wet gauze grips without squeezing. The extension along the dorsum of the thumb splint as well as giving a base for traction.

Absence of padding under these molds is essential. It permits the myriad hairs of arm and hand to serve as anchors. I have given up in all plaster work, the use of sheet wadding. When padding is necessary over bony points, and on plaster margins, sadder's felt or sponge rubber serves best. If no padding be needed none is used. A smoothly molded plaster is kinder to the skin than the undulating vagaries of sheet wadding.

The apparatus for reducing fractures of the radius and ulna is presented with distinct reservations. These fractures of both bones may be divided, therapeutically into two broad groups: those which respond to closed manipulation and those which do not. It is desirable that the first group be as large as possible. The use of good local or deep general anesthesia, manipulation under the fluoroscope, prolonged traction to tire spastic forearm muscles—these will increase its numbers. A certain proportion of cases must fall into the operative class.

In between are those that respond to skeletal traction. Let us add to their number a group of cases we have all met—the old, ill-treated, ununited fractures of radius and ulna.



Fig. 6. The patient holds the arm, unsupported, in abduction. The apparatus is not here.

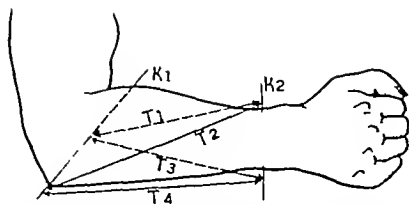


Fig 7 K_1 , Kirschner wire through the proximal end of the ulna, at right angles to K_2 through the distal ends of radius and ulna T_1, T_2, T_3, T_4 , turnbuckles

in which powerful flexor muscles have contracted and overcome the extensors to produce marked angulation at the site of the fracture—an angulation that must be corrected before good operative work can be done. It was in such cases that our turnbuckle apparatus (Fig 6) was first used. We have since used it in selected, fresh fractures, with good results.

Kirschner wires are used according to the common technique. One is drilled through the proximal end of the ulna, one through the distal ends of radius and ulna. These wires are at right angles to one another when the hand is midway between pronation and supination. (This is not only the position of optimum function, it is the position of best muscular balance and the one in which radius and ulna are most nearly parallel.)

On the Kirschner wires are mounted four turnbuckles (Fig 7, T_1, T_2, T_3, T_4). Thus they form four triangles of force, two with their bases on the radius-ulna wire, two with their bases on the olecranon wire. Manipulation of the fractured bones is possible in all planes. They are held stable in any position without further splinting.

The apparatus and its application in detail. Four $3\frac{1}{2}$ inch turnbuckles are used. These have a range between contraction and expansion, of $2\frac{1}{2}$ inches. Three sets of right hand threaded ends are made for each turnbuckle— $2\frac{1}{2}$ inch, $4\frac{1}{2}$ inch, $6\frac{1}{2}$ inch (Fig 8), giving for the set a continuous range from 5 to $11\frac{1}{2}$ inches, to fit children and adults. Channels are cut to the Kirschner wire openings in the right hand threaded ends to permit changing sizes, without opening the stirrup. This is rarely necessary. The right hand threaded ends are offset three-quarters of an inch to allow for the curve of the arm. On two of the

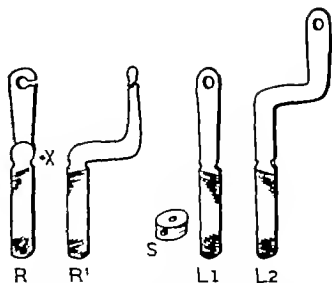


Fig 8 R, R^1 — $2\frac{1}{2}$ inch right hand threaded end for turnbuckles $4\frac{1}{2}$ inch and $6\frac{1}{2}$ inch pieces are identical, but lengthened at λ . L_1 , Left hand threaded ends for turnbuckles T_3 and T_4 . L_2 , Left hand threaded ends for turnbuckles T_1 and T_2 . S , Stop, with setscrew, for Kirschner wire

turnbuckles, for T_1 and T_2 , Figure 7, the left hand threaded ends are also offset $\frac{3}{4}$ inch, and are $\frac{3}{4}$ inch longer, to compensate for the added length of their diagonal direction. Four stops with set screws are provided to prevent the Kirschner wires from slipping in the bone if unequal stress be put on them.

The Kirschner wires are drilled through distal radius and ulna, and through the proximal ulna. Sterile, saddle's felt "washers" are mounted on each side of each wire, against the skin. The stops are set on the wires. The turnbuckles follow, the wires are drawn taut in stirrups. The proximal stirrup can be slung to the posterior surface of the upper arm by adhesive. The distal rests best on the dorsum of the forearm. The turnbuckles are now adjusted to reduce the fracture. Obviously, to correct bony angulation, lengthening of one turnbuckle will necessitate simultaneous lengthening of one other, and shortening of the remaining two. Thus, if there be an ulnar convexity, lengthening of T_1 and T_2 must be accompanied by shortening of T_3 and T_4 . Uniform traction is applied by making equal stress on all four. As with any form of screw traction, the danger of over extension must be guarded against. Fluoroscopic control of manipulations is desirable.

With a satisfactory reduction confirmed by x-ray examination, arm and apparatus may be supported in an ordinary sling. When the patient is in bed the arm should be supported on the chest by pads, otherwise there is danger of pressure on the medial stop on the



Fig. 9. Case 2. December 8, 1940

olecranon wire pushing it against the skin. The patient is allowed active movements of wrist and elbow (the latter is limited to 25 degrees). These movements are painless and seem to cause no abnormal mobility at the fracture line. Despite this apparently complete immobilization, I have not depended on the apparatus alone for splinting beyond the first two weeks. Perhaps this is an unnecessary precaution. I do not yet know. At the end of that time, turnbuckles are removed and plaster applied from the insertion of the deltoid to the proximal crease of the palm in incorporating the wires.

If desired plaster may be applied immediately following reduction. In this event it is better to use the large Kirschner stirrups, to facilitate the application of the plaster beneath the turnbuckles.

Three cases in which the use of the turnbuckles was particularly indicated.

CASE 1 (Victoria General Hospital, No. 26391. Fig. 6) The patient, aged 43 years, was admitted with fracture of radius and ulna in the middle third. Both fractures were oblique. The radius showed very slight displacement the ulnar fragments were overriding with angulation. The elbow joint was the seat of an osteoarthritis. To lessen the immobilization time of the elbow reduction was made with the turnbuckle apparatus and movements of elbow and wrist were permitted, for weeks. X-ray examination at this time showed early callus formation. A plaster was then applied from deltoid insertion to the proximal crease of the palm, incorporating the wires. The turnbuckle apparatus was removed.

CASE 2 (Victoria General Hospital, No. 26363) The patient, male, aged 26 years, was admitted with fracture of the radius and ulna in the upper and middle third of forearm. Standing union as fibrous. Flexor contraction had resulted in 70 degrees angulation.



Fig. 10. Case 3, February 1, 1941

lation at the site of the fracture (Fig. 9). Manual traction and massage were given (without result). December 9, 1940, the turnbuckle apparatus was applied. Adjustments were made to stretch the contracted muscles, the turnbuckles being given less turns every 2 or 3 days. February 5, 1941, the angulation was almost completely corrected (Fig. 10). The arm was prepared for operation to freshen the bone ends and fix them internally. After operation the apparatus was reapplied to prevent recurrence of contraction.

CASE 3 (Hullax Infirmary, No. 15030) The patient, male, aged 55 years, had an ununited fracture of the radius and ulna in their middle thirds. There was 5 degrees of ulnar convexity at the site. Operation was performed. The bones appeared healthy, the ends were freshened, perforated with multiple drill holes, and wired. The bones were held straight with little effort. Incisions were closed and plaster cast was applied over light dressings. X-ray films taken at the end of 3 weeks showed good callus formation but return of the angulation, although the cast had not been disturbed. The cast was removed. Kirschner wires and the turnbuckle apparatus were applied, the angulation was corrected and so held till firm bony union.

SUMMARY

Presented as useful adjuncts to fracture therapy are:

1. A spiral plaster mold for fractures of the lower end of the radius, the metacarpals and phalanges, which grips and immobilizes the part without causing circulatory interference.
2. An apparatus for reduction of fractures of radius and ulna which consists of four special turnbuckles mounted on Kirschner wires through distal radius and ulna, and through proximal ulna, so as to give control of the fragments in all planes.

THORACOSCOPY AND PNEUMOLYSIS

Observations on One Hundred Consecutive Cases

LOUIS CARP, M D, F A C S, and BORRIS A KORNBLITH, M D, F A C S,
New York, New York

RIVERSIDE HOSPITAL is one of the New York city municipal institutions for the tuberculous in which far advanced cases constituted about 72 per cent of the admissions during the past 5 years. During this same period 69 per cent of the patients were colored. In most of the cases pneumothorax therapy had been initiated elsewhere. In many instances thoracoscopy and pneumolysis were carried out as a last resort in patients with bilateral disease in the hope that some clinical improvement might be produced by cutting adhesions to help in the collapse of a cavity and the conversion of sputum. It is apparent, therefore, that we have had the more unfavorable type of material for these procedures. No patient was operated upon except after consultation with the medical service, directed by Dr. Max Taschman, and such specialty services as were indicated. We shall report our observations and follow-up notes on our first 100 consecutive patients who had thoracoscopy or pneumolysis.

TECHNIQUE

The instrument. About 95 per cent of the pneumolyses were performed with the Moore apparatus, by the use of thoracoscopy through one opening into the pneumothorax cavity and by division of the adhesions through another opening with an electrode which carried coagulating and cutting currents. The Coryllos instrument with its actual cautery was used for the remainder of the cases. All instruments are tested carefully before operation to make sure that the light bulb, cable connections, and current are in working order. On a number of occasions, unnecessary

bleeding was produced by a defective current as a result of improper electrical connections. A blurred field of vision may result from a moist ocular, from insufficient current, from a cold light bulb or observation lens or their moistening by blood or intrathoracic fluid. Appropriate measures correct all of these conditions.

The position of the patient. In most instances the patient was placed on his back with a pillow beneath the shoulders. The head was hyperextended and turned to the side opposite the operative field. The hand on the side of the operative field was placed beneath the head. There was no hesitation in sitting the patient up or turning the trunk if such positions produced a better view of the adhesions and easier intrathoracic manipulation.

Anesthesia. Local novocain anesthesia was used exclusively with especial care to infiltrate the parietal pleura.

Thoracoscopy openings. In over 90 per cent of the cases, openings into the second interspace in the midclavicular line and the third interspace in the midaxillary line were found adequate for thoracoscopy and pneumolysis. When indicated, openings were made in any other part of the chest wall. Stab wounds through the intercostal space permitted the snug introduction of the trocar and cannula. In this way postoperative emphysema of the chest wall and adjacent tissues was minimized or prevented, especially if the edges of the stab wound were tightly approximated by deep suture.

Division of adhesions. Pneumolysis requires patience and meticulous care and any attempt at hurry may produce a disastrous complication or incomplete therapy. The ideal time for cutting adhesions seemed to be as early as possible, when the mediastinum was already stabilized by the pneumothorax and when

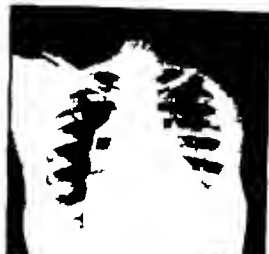
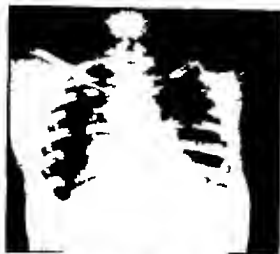


Fig. Successful collapse of cavity following pneumolysis. Colored female aged 35 years, duration of symptoms 6 months, duration of pneumothorax 3 months. a, Unilateral pulmonary tuberculosis with cavity 3 cm in diameter in right upper lobe. Note that are interpreted as 1. string adhesions running from the upper lobe toward the first rib. Thoracoscopy showed thick columnar adhesions which fanned out at the apex of the thoracic cage. Pneumolysis. b, Roentgenogram 27 days after operation 1. shows beginning collapse of the cavity aided by continued pneumothorax refills. Note spread of disease in the hilar region of the contralateral lung. This as temporary. c, Roentgenogram 9 months after operation 1. shows complete collapse of the cavity. The spurs as converted 4 months after operation. A 20 months follow-up shows involvement of the contralateral lung and partial expansion of the right upper lobe which contains cavity. Spurs as possible.

this was adequate for intrathoracic visualization and instrumental manipulation. Whenever possible we attempted to cut adhesion near the chest wall. At this point there is less danger of injury to lung and adjacent anatomical structures and usually there is less bleeding. At times enucleation of the adhesion from the chest wall was advisable. At other times partial pneumolysis was performed under the following conditions: technical difficulty, too lengthy an operation or a desire to stretch an incompletely divided adhesion by increased intrathoracic pressure

so that its complete division at a later date would be easier. Pneumolysis in stages was performed in 9 of our cases. In 5 of these there were 2 procedures and in 4 there were 3.

Postoperative care. Patients were kept in bed and given fluids for 24 hours with codeine for sedation and to diminish the cough reflex. Pneumothorax refills were continued within the first 24 hours after operation.

THE ADHESION

Location. We tried to correlate the locations of adhesions by roentgenogram and



2a



2b

Fig 2 Partial pneumolysis with subsequent bilateral pulmonary fibrosis and conversion of sputum. Colored female, aged 24 years, duration of symptoms, 6 months, duration of pneumothorax 3 months. a, Bilateral pulmonary tuberculosis, with cavity 3 centimeters in diameter in the right upper lobe. Note what was interpreted as massive apical adhesions and string adhesions running toward the second rib. Thoracoscopy showed thirteen string adhesions. Partial pneumolysis. Patient developed a right hydrothorax promptly and contralateral spontaneous pneumothorax 10 days after operation. b, Roentgenogram 3 weeks after operation to show partial collapse of the right upper lobe and fluid in the right pleural cavity. The sputum was converted at this time. c, Roentgenogram 15 months after operation to show re expansion of the lung and bilateral fibrosis. The patient is symptomatically improved and the result is probably not attributable to the original operative procedure.



2c

thoracoscopy. In about 90 per cent of the cases this correlation showed that the roentgenogram was only partially accurate, but it usually served as a guide for the position of the main adhesions. Usually, thoracoscopy showed more adhesions than indicated by

roentgenogram and very often the roentgenogram could not predict their direction. As a rule, mediastinal adhesions could not be visualized in the chest film.

Character and shape In the majority of the cases these could not be foretold by roent-



Fig. 3a.



Fig. 3b.



Fig. 3c.

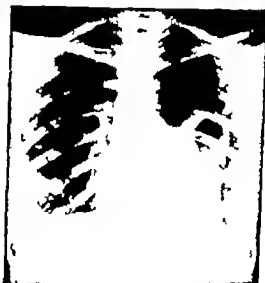


Fig. 3d.

genogram. The interpretation of what appeared to be a string adhesion in the film very often proved to be a thick, spool plicated or quadrangular adhesion. In other instances what looked like a divisible adhesion on the roentgenogram proved to be indivisible because of its character shape, or anatomical position or because of a complete synchia between the lung and chest wall. On the con-

trary what looked like an indivisible adhesion on the roentgenogram was often divisible. We have learned therefore that it is generally advisable to use thoracoscopy in order to determine the pathological state in the pneumothorax cavity and to decide at the time of operation whether pneumolysis is feasible. Adhesions, according to shape, conformed to the following descriptions in their order of fre-

Fig 3 Three stage pneumolysis with collapse of large cavity and conversion of sputum. Colored female, aged 30 years, duration of symptoms, 3 months, duration of pneumothorax, 2 months. a, Unilateral pulmonary tuberculosis with left apical cavity 4 centimeters in diameter and what was interpreted to be a cord adhesion running toward the first rib and massive adhesions between the upper lobe and the mediastinum. Partial pneumolysis with division of one cord adhesion. b, Roentgenogram 6 days later to show the cavity still suspended by what appeared to be a cord adhesion. Thoracoscopy 2 months after the first operation showed tubercles on the surface of the lung. Pneumolysis of two more adhesions. c, Roentgenogram 1 month later to show what appeared to be a cord adhesion running from the apex of the cavity to the mediastinum and another adhesion running from the lateral border of the cavity to the first interspace. The cavity has dropped and there is a small amount of fluid in the pleural cavity. Pneumolysis of these adhesions 8 days later. This was the third operative procedure. d, Roentgenogram 6 days later and 4 months after the first operation to show complete division of the restraining adhesions with release of the upper lobe and re expansion of the left lower lobe. e, Roentgenogram 15 months later and 18 months after the first operation to show collapse of the cavity. The sputum was converted 6 months after the last operation.



Fig 3c

quency (Table I) string, fan, cord, spool, synechia, pyramidal, quadrangular, band

OBSERVATIONS FROM STATISTICAL ANALYSIS

The following represents some of the more important observations resulting from analysis of our statistical data.

Among 100 consecutive cases that came to operation there were 32 complete pneumolyses, 43 partial pneumolyses and 25 thoracoscopies (Table II). By complete pneumolysis we mean the division of all visible restraining adhesions. By partial pneumolysis we mean an incomplete division of one or more adhesions, or the complete division of a fraction of the total number of adhesions visualized. The average age for the entire series was 29 years, the youngest patient was 14 and the oldest 53 years. Thirty per cent were males and 70 per cent females. Eighty-nine per cent were of the colored race and 11 per cent were white. The average duration of symptoms on admission to the hospital was 11.28 months. At the time of operation, the average duration of the disease was 18 months and the average duration of the pneumothorax was 7½ months. On admission, the sputum was positive for tubercle bacilli in all of the patients. At the time of operation the sputum was positive in 88 per

cent of the cases with evidence of cavitation in all. Cavities had an average diameter of 3.5 centimeters. Seventy-six per cent of the patients had bilateral disease and in the remaining 24 per cent it was unilateral (Table III). The average estimated extent of the pneumothorax was about 60 per cent, the smallest 30 per cent, and the largest 90 per cent. Two hundred and ninety-seven adhesions were seen at operation, and 60 per cent of these were divisible. Besides adhesions, thoracoscopy demonstrated the aorta, the subclavian and innominate vessels, the beating heart and the pericardium, the phrenic and vagus nerves, fibrin bodies, purulent and nonpurulent fluid, tubercles and fibrinous exudate on the visceral pleura, and the diaphragm (Table IV).

In the 32 patients who had complete pneumolysis, the sputum was converted and the cavity closed in 62 per cent. In 4 per cent the sputum was converted but the cavity remained open. The cavities collapsed in an average time of 36 days and the sputum was converted in an average time of 60 days. In the 43 cases which had a partial pneumolysis, the sputum was converted and the cavity closed in 30 per cent. The cavities collapsed in an average time of 64 days and the sputum was converted in an average time of 75 days.

TABLE I.—THOROSCOPIC TYPES OF ADHESIONS

	Complete pneumothorax	Partial pneumothorax	Thoracoscopy only	Grand total	
				No.	Per cent
Free collapsed		49			
Cured	14			14	6
Stripped			8	94	33
Spont.	8	14		22	
Pyramidal			14		
Columnar					
Quadrilateral					
Band					3
Spontaneous				20	7
Total	22	63	32	297	100

In the 25 cases which had thoracoscopy, the sputum was converted and the cavity closed in 36 per cent. The cavities collapsed in an average time of 110 days and the sputum was converted in an average time of 90 days. The reasons for these last results after thoracoscopy were increased pressures from fluid or pneumothorax, spontaneous rupture of adhesions, pleuropneumonia, and spontaneous fibrosis and recession of the disease. It becomes apparent therefore that the length of time for the closure of cavities and conversion of sputum increases in the procedure in the following order: complete pneumothorax, partial pneumolysis and thoracoscopy. We have

TABLE III.—DISTRIBUTION OF PULMONARY LESIONS

	Complete pneumothorax		Partial pneumothorax		Thoracoscopy only		Grand total	
	right	left	right	left	right	left	No.	Per cent
A. Unilateral disease with cavity no pleural fluid								
Unilateral disease with cavity with pleural fluid								
Total								
C. Bilateral disease with cavity no pleural fluid	20		14				34	58
D. Bilateral disease with cavity with pleural fluid							16	
Total							50	76
Total	18	14	19	4	3	11	59	100

TABLE II.—FOLLOW UP RESULTS

	Complete pneumolysis 21 cases Per cent	Partial pneumolysis 3 cases Per cent	Thoracoscopy only 25 cases Per cent
Sputum converted	47	30	36
Cav. closed	62	30	36
Improved	37	25	25
Sputum positive		20	64
Cav. open	37	60	64
Unimproved	3		
Complications	26	70	64
Died	26	20	77

also noted that conversion of sputum usually occurs about a month after the collapse of the cavity.

Seventy-one per cent of all the cases had complications which were similar in all 3 procedures. At first glance this percentage seems unusually high, but we have included cases with innocuous hydrothorax which constituted almost half of all the complications. These in their order of frequency were hydrothorax (innocuous), spread of infection to the contralateral lung, tuberculous empyema, spontaneous pneumothorax, hemoptysis, hemothorax, and pleurocutaneous fistula.

Tuberculous empyema occurred in 19 per cent of the entire series and mixed infection in 3 per cent. Only 2 of the entire group occurred directly after operation. Seven of

TABLE IV.—ADDITIONAL THOROSCOPIC FINDINGS

	Complete pneumolysis	Partial pneumolysis	Thoracoscopy only	Grand Total	
				No.	Per cent
Adhesions to pleural cavity			3		1
Fibrous bands					
Tubercles or tubercular plaques					
Fluid in pleural cavity					
Adhesions to parietal					
Lung covered with fibrin and tubercles				20	20
Visceral adhesions					
Adhesions to mediastinal vessels					

TABLE V — POSTOPERATIVE COMPLICATIONS

	Complete pneumolysis		Partial pneumolysis		Thoracoscopy only		Grand total	
	No	per cent	No	per cent	No	per cent	No	per cent
Total number	25	78	30	70	16	64	71	71
No complications	7	22	13	30	9	36	29	29
Early complications 1-2 months postoperatively								
Hydrothorax	8	24	15	37.5	7	28	30	30
Tuberculous empyema	1	3	1	2.5	0	0	2	2
Spread to contralateral lung	2	6	1	2.5	1	4	4	4
Hemothorax	2	6	0	0	0	0	2	2
Spontaneous pneumothorax	1	3	0	0	0	0	1	1
Total							37	
Late complications—2-31 months postoperatively								
Hydrothorax	4	12	5	12.5	2	8	11	11
Empyema								
Tuberculous	5	15	5	12.5	7	28	17	17
Mixed	2	6	1	2.5	0	0	3	3
Pleurocutaneous fistula	2	6	1	2.5	0	0	3	3
Spread to contralateral lung	4	12	11	27.5	2	8	17	17
Spontaneous pneumothorax	5	15	4	10	0	0	9	9
Hemoptysis	1	3	0	0	2	8	3	3
Tuberculosis of chest wall at site of trocar opening	1	3	0	0	0	0	1	1
Tuberculous laryngitis	2	6	1	2.5	1	4	4	4
Tuberculous enterocolitis	1	3	2	5	1	4	4	4
Total							63	
Died	9	28.2	11	26	7	28	27	27

TABLE VI — CAUSES OF DEATH

	Complete pneumolysis		Partial pneumolysis		Thoracoscopy only		Grand total	
	No	Per cent	No	Per cent	No	Per cent	No	Per cent
Type of disease								
Unilateral	0		0		0		0	
Bilateral	9	28	11	26	7	28	27	27
Spontaneous pneumothorax, tuberculous empyema, bronchopleuro cutaneous fistula	3		0		0		3	
Spread of disease in both lungs	3		9		2		14	
Tuberculous empyema	2 (*)		2		0		4	
Spontaneous pneumothorax	1 *		0		0		1	
Hemothorax	0		1 *		1		2	
Tuberculous laryngitis	0		1		1		2	
Tuberculous enterocolitis	0		1		1		2	
Hemoptysis from opposite lung	0		0		1		1	
Cardiac failure	0		0		1		1	

*Operative deaths

Spread of the disease in both lungs, 14, tuberculous empyema, 4, spontaneous pneumothorax, tuberculous empyema, bronchopleurocutaneous fistula, 3, hemothorax, 2, hemoptysis, 1, spontaneous pneumothorax, 1, and cardiac failure, 1. There were 3 deaths which could be attributed to the operative procedure. One patient died during operation from hemorrhage produced by injury to one of the large blood vessels by the electrode.

TABLE VII — RESULTS OF SPUTUM EXAMINATION

	Complete pneumolysis		Partial pneumolysis		Thoracoscopy only		Grand total	
	No	Per cent	No	Per cent	No	Per cent	No	Per cent
Converted from positive to negative	14	67	12	30	9	36	35	40
Remained positive	9	33	28	70	16	64	53	60
Total	23		40		25		88	100
Sputum negative before operation	9		3		0		12	

Progress of Cavity

Cavity closed	20	62.5	13	30.2	9	36	42	42
Cavity remained open	12	37.5	30	69.8	16	64	58	58

the 22 empyemas followed thoracoscopy (Table V)

There were 7 cases of spontaneous pneumothorax and they predominated after complete pneumolysis. This complication arose early only once after the operative procedure (Tables IV and V). Postoperative emphysema was not troublesome.

The average follow-up time was 10 months in all the cases the longest period being 28 months the shortest 1 month.

The early and late death rate in the entire group was 27 per cent, and it was practically identical in complete or partial pneumolysis and in thoracoscopy. The causes of death in their order of frequency were

VIII.—COMPARISON OF PERIOD OF TIME ELAPSED BETWEEN OPERATIVE PROCEDURE, CLOSURE OF CAVITY AND CONVERSION OF SPUTUM

	Days after complete pneumolysis	Days after partial pneumolysis	Days after thoracoscopy only	Grand average days
Cavity collapsed				
Average period	36	64	30	30
Shortest period			60	
Longest period	120	120	30	120
Sputum converted				
Average period	60		90	75
Shortest period		30	60	
Longest period	20	60	60	120

This occurred early in our experience. Another death occurred 2 months after operation from hemothorax with empyema which developed 6 days after operation. There was no bleeding at the time of operation. A third patient died from spontaneous pneumothorax 10 days after operation. Of the 27 patients with bilateral disease 24 died from causes not due to operation, in an average time of 9 months (Table VI).

Before operation, 12 patients had a negative sputum despite cavitation with adhesions. It seemed advisable to cut these adhesions. One patient developed a contralateral spread of the disease with a hydropneumothorax. Nine months later the sputum became positive and a tuberculous empyema developed on the side operated upon. Another patient had a persistently negative sputum for 6 months after pneumolysis. This patient died of a spontaneous pneumothorax on the contralateral side.

Tubercles without accompanying empyema could be visualized beneath the visceral pleura in 15 per cent of the cases. Over a follow up period of from 4 to 28 months 2 of these patients developed pleural fluid which contained tubercle bacilli. In 1 case the fluid appeared 11 months after partial pneumolysis and in the other patient it appeared 5 weeks after thoracoscopy. Aspiration therapy helped in the disappearance of the fluid in both cases. We believe, therefore, that tubercles on the surface of the lung do not contraindicate pneumolysis, unless they are subject to injury by the electrode.

SUMMARY

1. Our observations are based on complete or partial pneumolysis or thoracoscopy in our first 100 consecutive cases of pulmonary tuberculosis among whom 76 per cent were classified as far advanced and 89 per cent were of the colored race.

2. In most of the patients pneumothorax therapy had been initiated elsewhere so that the average duration of this therapy was 7½ months before operation. This period is far too long if more successful results are to be obtained. Restraining adhesions should be cut as soon as the pneumothorax has stabilized the mediastinum and when it is adequate for visualization and intrathoracic manipulation of instruments.

3. The roentgenogram of the chest served only as a guide for the approximate location, shape, and potential divisibility of adhesions, but it did not predict these with any degree of accuracy.

4. Thoracoscopy and electrode openings were usually found to be adequate when made in the second intercostal space in the midclavicular line and in the third intercostal space in the midaxillary line.

5. Thoracoscopy is advisable to determine the pathological state in the pneumothorax cavity and also the feasibility of pneumolysis. Thoracoscopic findings are enumerated.

6. The presence of subpleural tubercles does not necessarily mean that they will rupture into the pleural cavity. They do not therefore contraindicate pneumolysis, unless tubercles present in adhesions are subject to direct injury by the electrode.

7. The complications after all three procedures are enumerated, with special reference to tuberculous empyema.

8. Comparative statistics indicate that complete pneumolysis was followed by conversion of sputum and closure of cavities in about two-thirds of the procedures and that partial pneumolysis or thoracoscopy accomplished the same results in about one-third of the procedures. The length of time for closure of cavities and the conversion of sputum increased in these procedures in the following order: complete pneumolysis, partial pneumolysis and thoracoscopy. The

version of sputum occurred about 1 month after the collapse of the cavity

9 In our entire series of 100 cases, 40 patients had a favorable outcome following all the procedures. The cavities closed, the sputum was converted and there was symptomatic improvement. The average follow-up time was 10 months.

10 If it is generally accepted that 90 per cent of patients with cavitation and restraining adhesions will die without operative intervention, then our statistics indicate that even in far advanced cases partial or complete pneumolysis reduces the mortality considerably.

11 There was a 3 per cent operative mortality and the causes of death are given. The

remaining 24 per cent, all of whom had bilateral disease, died from causes not attributed to operation, in an average time of 9 months.

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CONTINUOUS—SERIAL FRACTIONAL CONTROLLABLE, INTERMITTENT—SPINAL ANESTHESIA

With Observation on 1000 Cases

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SINCE April 10, 1939, when we gave the first continuous spinal anesthetic, we have administered more than 1,250 entirely satisfactory anesthetics by this method. In this paper we are giving some of our observations and a statistical report on 1,000 cases.

In this series of cases we have used novocain (procaine hydrochloride) as the anesthetic agent. Our choice of this drug has been deliberate since it is the least toxic of all drugs used in producing anesthesia by injection into the subarachnoid space. By the method of spinal anesthesia we employ, we are able to give just sufficient dosage to produce anesthesia to the desired level and degree. This anesthesia is maintained as long as necessary by adding subsequent small doses as they are needed. We have thereby changed the method of spinal anesthesia from the "single dose" to the "fractional dose" technique which now places spinal anesthesia in the same category with other anesthetics administered by the continuous or fractional dose method such as intravenous anesthesia, ether, cyclopropane, nitrous oxide, etc.

Safety and controllability are the two things we desire most in spinal anesthesia. Sise has pointed out that the first 30 minutes of spinal anesthesia are the most dangerous. It is during this period that deaths and complications are most likely to occur and especially is this true when a single large dose of a toxic drug is administered. We believe that by giving much smaller initial doses of the drug it

should increase the safety. When the needle is left in the subarachnoid space the drug can be rapidly recovered by withdrawing a sufficient quantity (5 to 10 cubic centimeters) of cerebrospinal fluid if untoward toxic symptoms develop, especially in those patients who are very sensitive to the drug. The toxic symptoms seen following injection of a drug into the subarachnoid space are not due to the drug that is fixed in the lipid elements of the sensory and motor synapses producing anesthesia but are due to the absorption of the drug from the cerebrospinal fluid into the systemic (venous) circulation. (This factor will be further emphasized when we deal with spinal anesthesia used in thoracic surgical procedures.) The respiratory center is the most vulnerable to attack. When and if toxic symptoms of an alarming character develop, the first thing to do is to withdraw rapidly the cerebrospinal fluid containing the toxic agent. The greatest concentration of the drug is in the vicinity of the point of the needle. The nerves promptly recover from the anesthesia. This observation was first made accidentally when a turned stopcock on the syringe permitted an unintentional escape of cerebrospinal fluid into the syringe with a subsequent loss of anesthesia. This phenomenon has since been confirmed on numerous occasions. Spinal anesthesia is maintained by the drug that is present in the cerebrospinal fluid and when the concentration of this drug falls below a definite level the anesthesia promptly wears off. After anesthesia is established it takes relatively small doses to maintain the anesthesia for any desired length of time. If we are doing serious technical operative procedures and it is important to maintain complete relaxation at all times, we give an additional dose of 50

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milligrams of novocain (5 per cent) solution at the expiration of every 30 minutes. Otherwise, we wait for the initial or previous dose to show signs of wearing off before we give an additional injection.

With a single exception anesthesia was produced to the desired level and degree and the operation was completed under spinal anesthesia. The exception here referred to was a case in which the right middle and lower lobes were being removed for bronchogenic carcinoma and while sensory anesthesia was present up to the level of the hyoid bone, a persistent cough, induced by the incidental tugging on the bronchus, could not be controlled. In this instance cyclopropane was used for this part of the operation. In no other case was a supplementary anesthetic necessary. There were no anesthetic fatalities and no neurological complications. Toxic symptoms were promptly controlled by withdrawal of the drug by rapid aspiration of spinal fluid (3 to 10 cubic centimeters) and by giving inhalations of oxygen.

Some of the disadvantages of the single dose method of spinal anesthesia are (1) failure of the drug to "take" or produce anesthesia to the desired level or degree, (2) the action of the drug wearing off before the operation is completed, and, (3) toxic symptoms or even sudden death following the intraspinal administration of a large dose of a toxic drug. In this series of cases we have eliminated these disadvantages by using this new method of spinal anesthesia.

From the clinical and experimental standpoints, it is generally accepted that procaine hydrochloride is the least toxic of all drugs used to produce spinal anesthesia. Its action is also of the shortest duration. The drugs employed in producing spinal anesthesia, which have a more prolonged action, are also found to be more toxic. There is no reason why any drug or combination of drugs used in producing spinal anesthesia cannot be used by the "fractional" dose or continuous method. It should be more safe to use them by this method than by the single dose technique since the patient would be exposed to smaller amounts of the drug, and because the drug could be recovered by aspiration of a suffi-

cient amount of spinal fluid containing it, should alarming symptoms develop and make this action necessary.

Novocain produces anesthesia promptly when introduced, in sufficient quantity, into the subarachnoid space. We have observed that it takes approximately 90 seconds to relieve pain completely and produce muscular relaxation when it is given in subsequent injections. We feel that each patient is a case unto himself and that each has an individual response to novocain. We have observed a case in which the anesthetic action of novocain disappeared every 15 minutes while doses of 100 milligrams each were being used. We have had anesthesia with 50 milligrams of novocain last for an operation that required 1 hour and 45 minutes. Subsequent injections of 50 milligrams each last approximately 30 minutes, producing both motor relaxation and sensory block. By injecting small doses of novocain (15 to 20 mgm) into the subarachnoid space we have been able to produce sensory block (anesthesia) without causing motor paralysis. In the case of an elderly woman with a strangulated hernia we produced satisfactory anesthesia with 30 milligrams. We are of the opinion that by using this method of anesthesia it is possible to lower the morbidity and mortality rates, especially in serious and prolonged surgical procedures.

TECHNIQUE

Equipment Figure 1 illustrates the equipment used.

1 *a*, Indicates the head end of pad used in continuous anesthesia, *b*, the break in the pad for detachment when perineal operations are done, *c* and *c'*, the break in pad for bending at knees when patient is in Trendelenburg position—as suggested by M. J. Nicholson of the Lahey Clinic, *d*, the position of malleable needle left in subarachnoid space of patient when he is lying on back, *e*, the 30 inches of very small caliber thick walled rubber tubing connecting the 10 cubic centimeter Luer-Lok syringe to malleable needle in patient's spine.

2 Close-up of syringe, stopcock, rubber tubing and needle. *a*, Shows the stopcock connecting the Luer-Lok 10 cubic centimeter syringe and the rubber tubing, *b*, the rubber

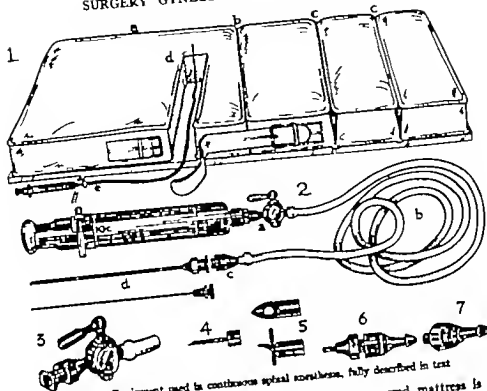


Fig. Equipment used in continuous spinal anesthesia, fully described in text

tubing—approximately 30 inches & the Luer Lok connecting rubber tubing and malleable needle & malleable needle

3 Close-up of stopcock.

4. Needle introducer or needle guide used in puncturing the skin

5. A short bevel with counter opening in the bevel of the malleable needle. This counter opening prevents blockage of the bevel by the meninges, and insures a free flow of spinal fluid

6 Luer Lok plug connected to spinal needle to prevent loss of cerebrospinal fluid

7 Luer Lok plug

Administration. In continuous spinal anesthesia we employ a short acting agent, procaine hydrochloride, which is injected in fractional doses as needed during operation. The patient is placed on a specially designed mattress and a very flexible, special alloy lumbar puncture needle remains in place in the subarachnoid space. This needle is connected to a syringe by means of a 30 inch piece of rubber tubing which is provided with Luer Lok connections at both ends.

The rubber covered mattress is 5 inches thick, 18 inches wide and 6 feet long (see 1 in Fig 1). It has a cut-out area 7 inches in length that comes under the lumbar spine when the patient is supine. There is a break in the center of the mattress, so that the part which supports the legs may be detached for perineal operations. Provision has also been made to break the lower part of the mattress to allow the feet to be dropped when a deep Trendelenburg position is desired (Fig 1 1c and 1d). If an abdominal operation follows the perineal operation, the patient may be pulled back into position and the lower half of the mattress replaced and made secure with straps and buckles (Fig 1 1b).

The spinal puncture is made with the patient in the left lateral decubitus position so that his back is toward the side of the mattress with the gap in it. The malleable special alloy needles are made in 3 sizes No. 17 No. 18, and No. 19 gauge. We prefer No. 18 gauge needles. The site selected for spinal puncture depends upon the site of operation—the second or third for upper abdominal procedures,

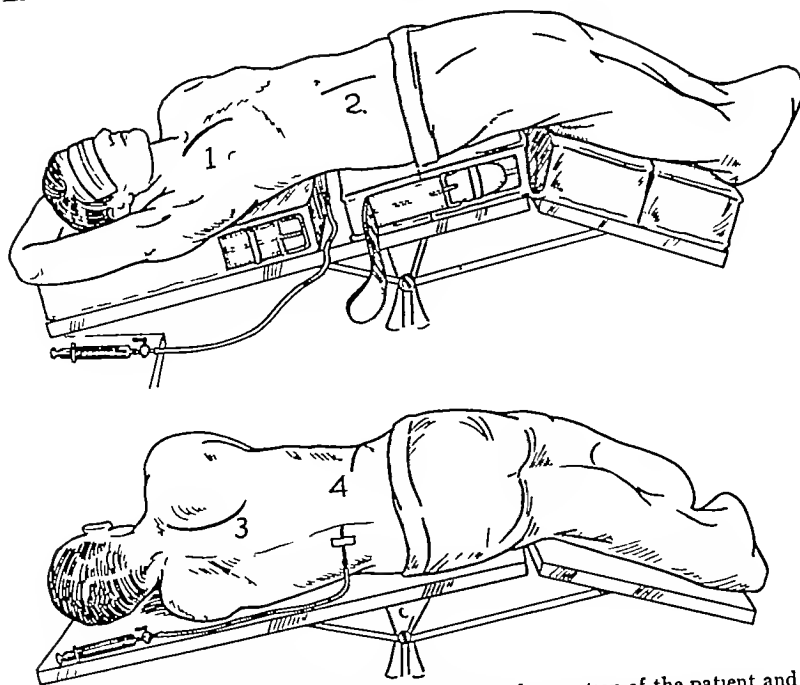


Fig 2 A diagrammatic drawing demonstrating the position of the patient and the continuous spinal apparatus in place 1, 2, 3, and 4, Represent incisions for the surgical procedures in these areas

the third or fourth for lower abdominal operations, and the fourth or fifth for operations on the perineum, rectum, and lower extremities. A Sise introducer is used to puncture the skin, and, on withdrawal leaves a track for the soft malleable special alloy needle to traverse. When the cerebrospinal fluid escapes from the hub of the needle, a 10 cubic centimeter Luer-Lok syringe is connected with it, and enough fluid is withdrawn to make up a 5 per cent solution. We have 300 and 500 milligram ampuls of novocain. For estimated short operations we use 300 milligrams of novocain, dissolved in 6 cubic centimeters of cerebrospinal fluid. For long operations we dissolve 500 milligrams novocain in 10 cubic centimeters of spinal fluid. The syringe is disconnected and the needle is plugged to prevent a loss of spinal fluid. Generally, 500 milligrams of novocain is dissolved in 10 cubic centimeters of spinal fluid to make a 5 per cent solution, which contains 50 milligrams per cubic centimeter. The syringe with the stopcock attached is connected to one end of the 30 inches of thick walled, small bore, rubber

tubing. The stopcock is opened and 2 cubic centimeters of the mixture is forced into the tubing, thus displacing the air and completely filling the tube. Then the stopcock is closed. The Luer-Lok connection at the opposite end of the tubing is securely connected to the needle which was left in the spine. The stopcock is opened and 2 to 3 cubic centimeters of the mixture is introduced into the subarachnoid space and the stopcock is closed.

With the needle left in place, the patient is gently turned on his back so that the needle points downward in the center of the gap in the pad. It should not touch the table or mattress at any time. The patient should be kept in 5 degree Trendelenburg position during the induction period. When the height of anesthesia is tested and the desired level is not obtained in 10 minutes an additional injection, usually of 1 cubic centimeter is made. The height of the anesthesia can be extended and controlled by the following means: position of patient, volumetric dilution of anesthetic agent (barbotage), rate of injection, and total dosage of drug.

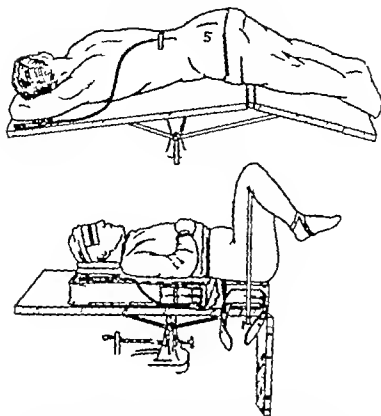


Fig. 3 The patient lying face down and the spinal needle bent to the side and secured with adhesive. This position used for such operations as excision of the coccyx, and medial operations. The lower drawing shows the lower half of the pad removed and the patient in lithotomy position.

Once anesthesia is obtained, it is easily prolonged by small fractional injections when needed, and we have a setup comparable to the one existing when ether is given by the open drop method or when pentothal sodium is given by the fractional dose intravenous technique. As the anesthesia begins to wear off it is so indicated by the fact that the intestines become less contracted, the abdominal muscles grow more tense, and the patient complains of abdominal discomfort or pain. Just as we would add more ether under similar circumstances to produce relaxation during inhalation anesthesia, when this occurs during continuous spinal anesthesia we give a small additional dose of novocain usually 50 milligrams. We have noted that it takes approximately 90 seconds for this added dose to exert its full effect. We now give these additional

doses, in longer operative procedures, at fairly regular anticipated intervals (usually every 30 to 40 minutes) and are provided with uninterrupted ideal operating conditions throughout the operation.

Preoperative medication. We consider the preoperative medication to be of great importance. On the evening before operation the patient receives 3 grains of nembutal. Three hours before operation the patient is given a second dose of 3 grains of nembutal by mouth. One hour before operation a hypodermic of $\frac{3}{4}$ grain morphine and $\frac{1}{100}$ grain of scopolamine is given. If the sedation is not sufficient, $\frac{3}{4}$ grain of morphine is given intravenously or hypodermically as often as is necessary during the operation. By using proper sedation the patients are spared the unpleasant memories sometimes accompanying

such an experience Most of them sleep throughout the operative period and afterward for many hours

During long and difficult procedures an intravenous injection of 10 per cent glucose solution is given via a vein in the leg These patients also receive a blood transfusion at the end of operation if it is indicated We make an effort to prevent and combat shock rather than wait until its onset before treatment is begun

ANALYSIS OF CASES

We are presenting a report on the first 1,000 cases in which this method has been used The operations in this series include 970 below the abdominal diaphragm and 30 above it In only a single case of the latter group was there a supplementary anesthetic used and that in a case of uncontrolled cough during the course of a pulmonary lobectomy In this case cyclopropane was used during the stage in which tugging on the bronchus precipitated the cough Sensory anesthesia in this case was at the level of the hyoid bone In all of the other cases the operation was begun and finished under spinal anesthesia, and no general or other anesthetizing agent was used

Age The average age for this group was 37.2 years The oldest patient was 83 years old and the youngest was 7 years of age We did an appendectomy on the latter and a leg amputation on the former Younger children do not give satisfactory co-operation to permit the extensive use of spinal anesthesia in that age group (under 7 years)

Length of operation The average length of the operations in this series was 50.4 minutes A total gastrectomy required 215 minutes (3 hours and 35 minutes) The shortest procedure took only about 2 minutes for the incision and drainage of an abscess One of our colleagues reported using this method to produce satisfactory anesthesia during the entire course of a gastrectomy requiring 6 hours

Dosage For these 1,000 cases the average total dose of novocain was 219.9 milligrams In the operations done above the diaphragm the dosage was much larger than the general average, being 445 milligrams This high figure influences the total percentage considerably for it is seen that in the remaining 970

cases the average total dosage was only 181 milligrams of novocain The average number of injections was 2.4 It is interesting to compare the average total dose of the first 500 cases which was 242 milligrams with that of the second 500 cases which was 198 milligrams We feel that this reduction in amount of total dose is due to our increased experience The largest dose given to any one patient was 2,200 milligrams This patient had had an earlier operation in which she required 1,800 milligrams of novocain to produce anesthesia This would indicate an individual tolerance and points out, too, that the dose in any given case is *enough* The smallest dose was 20 milligrams of novocain for amputation of a toe

We have used various dilutions from 1 per cent to 10 per cent solutions of novocain We have obtained best results from using a 5 per cent solution of novocain At times we have used previously prepared solutions of novocain in distilled water and while anesthesia was obtained the results were not always as satisfactory as when the solutions of novocain crystals in spinal fluid were used In thoracic surgical procedures we generally employ a dilution of 1 to 3 per cent This will be discussed more completely in a later paper

Effect on blood pressure The average systolic blood pressure at the beginning of operation for this series was 125.9 millimeters of mercury The average systolic pressure at the end of operation was 113.9 millimeters of mercury This indicates that there was an average fall in systolic blood pressure of only 12 points The blood pressure was recorded every 5 minutes of the operation It was noted that soon after the patient received the preliminary injection of ephedrine sulfate and novocain used to anesthetize the skin and support the blood pressure, there was a general elevation of the blood pressure but after the operation was in progress, the pressure had a tendency to become constant or to fall below that at the onset The average high blood pressure was 129.9 The average low was 103.4 A woman operated upon for a strangulated hernia had a blood pressure of 240 at the beginning and 170 at the end of operation She received 150 milligrams of novocain in 2

injections. In several instances the blood pressure fell to a systolic of 40 millimeters of mercury. We rarely use vasoconstrictors in these conditions but have found that venoclysis or blood transfusion affords the best relief. Most of these patients leave the operating room in good condition. They have a dry skin and a full pulse of good quality.

Morbidities Headache. This is a difficult thing to understand and hard to explain. In cases of the most simple nature we have had this complaint. Some patients subjected to longer operations had no subsequent headache. Our incidence of headache after spinal anesthesia is 2.8 per cent which approximately corresponds to the incidence seen by the former angle injection method. We call attention to the fact that we had 150 consecutive cases in which there were no postoperative headaches. In most instances this complaint is relieved by the use of aspirin or by lowering the head of the patient.

Urinary difficulty. There is no greater incidence of urinary retention with this method than with the ordinary method of spinal anesthesia. Our incidence of urinary retention was 3.4 per cent. In some of our plastic or pelvic operations we inserted an indwelling catheter for the first few postoperative days so that these patients do not enter into our statistics.

Pulmonary. There were 34 cases of pulmonary complications, 19 of these were bronchopneumonia, 9 were lobar pneumonia, 4 were atelectasis, and 2 were pulmonary embolism.

Nervous. There were no motor or sensory disturbances, no cranial nerve palsies or other neurological phenomena. A number of these patients have been observed for more than 3 years.

Mortality. There were 47 deaths among this series of 1,000 cases, making the gross mortality of 4.7 per cent. The average time that elapsed between operation and death was 6.9 days. In none of these deaths do we believe that the anesthesia was a contributing factor. Of the 47 who died 24 were suffering with malignant growths. There were 9 deaths from diffuse peritonitis. Among the remaining factors causing death were pulmonary, cardiac, and

renal conditions. From several others using this method we are informed of something more than 1,000 additional cases in which continuous spinal anesthesia was used. These added to our series make a known total of more than 2,000 cases. There has not been a death reported from the use of continuous spinal anesthesia.

Table I is an outline of the 1,000 cases in this series.

TABLE I.—OUTLINE OF 1,000 CASES DONE UNDER CONTINUOUS SPINAL ANESTHESIA

	Number
Gastrointestinal operations	
Stomach	46
Appendix	145
Intestinal and colon	45
Biliary tract operations	90
Hernia operations	
Sympathetic nervous system operations	3
Gynecologic operations	
Perineal	58
Abdominoperineal	51
Abdominal	83
Obstetric operations	42
Urologic operations	15
Proctologic operations	40
Cardiovascular operations	3
Thoracic operations	24
Orthopedic operations	40
Miscellaneous operations	5

Classification

	Exam-ined	Number	Total
Gastrointestinal operations			374
Stomach operations		46	
Total gastrectomy		4	
Subtotal gastrectomy and appendectomy		9	
Anterior gastroanastomosis		3	
Closure duodenal ulcer			
cholecystectomy and appendectomy		2	
Closure spontaneous rupture of stomach			
Reaction bleeding gastric ulcer			
Cholecystogastrostomy			
Biopsy carcinoma of stomach			
Biopsy head of pancreas			
Subtotal gastrectomy and cholecystectomy		5	
Closure perforated ulcer		4	
Closure perforated gastric carcinoma			
Appendix operations		145	
Appendectomy		33	
Appendicidal abscesses and drainage		7	
Appendectomy and excision of uric acid cyst		13	
Appendectomy and sigmoido-sphincterectomy		4	
Appendectomy and oteric suspension			

TABLE I.—Continued

Classification

	Non- lum.	Non- lum.	Total
Proctologic operations.			40
Hemorrhoidectomy		26	
Excision of fistula in ano		9	
Excision and drainage ischioanal abscess			
Biopsy fulguration of anorectal tuberculosis			
Fulguration of anorectal tuberculosis			
Cardiovascular operations			3
Ligation of patent ductus arteriosus.			
External iliofemoral arteriovenous anastomosis			
Right femoral embolectomy			
Thoracic operations			26
Reversion of esophagus			
Anterior thoracoplasty 1st stage		6	
Posterior thoracoplasty 1st stage		5	
Posterior thoracoplasty 2nd stage		6	
Posterior thoracoplasty 3rd stage		3	
Posterior thoracoplasty 4th stage			
Lobectomy			
Pneumonectomy			
Orthopedic operations.			40
Sequestrectomy osteomyelitis			
Excision of head of metatarsal		1	
Bilateral amputation of hammer toe			
Excision lateral sesamoid cartilage.		4	

TABLE I.—Continued

Classification

	Non- lum.	Non- lum.	Total
Excision palmaris stress.		20	
Excision of benign tumor of leg.		6	
Excision of rectum			
Amputation at mid-thigh		1	
Miscellaneous operations			5
Repair of eversion		2	
Excision and drainage of abscess		1	
Lipectomy and ventral herniorrhaphy			

SUMMARY

1 We are reporting 1,000 surgical cases in which operation was done under continuous spinal anesthesia.

2 We have discussed the technique employed in the use of this method and have presented some of the important observations in this series.

3 We wish to emphasize the safety and controllability of this method.

4. We feel that the morbidity and mortality can be lowered by the use of continuous spinal anesthesia.

TOTAL VERSUS SUBTOTAL HYSTERECTOMY FOR BENIGN CONDITIONS

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FOR years the question of whether the cervix should be removed along with the fundus in performance of supra-vaginal hysterectomy has created much discussion. Even among those surgeons who advocate total hysterectomy the technique in performing this operation is noticeably variable and each method has its own adherents who hold certain fixed opinions as to the results.

This paper is based on a group of 2,684 cases observed consecutively at the Mayo Clinic from 1935 to 1939, inclusive, in which operation was performed for benign conditions of the uterus. In 1,920 cases the surgical procedure was total hysterectomy and in 764, subtotal hysterectomy. Further subdivision was made into several classes, the patients who had similar physical hazards—obesity, anemia, and so forth—were placed in separate groups and these groups were analyzed for the occurrence of complications that arose in each. The object of the study was to detect any relation of cause and effect that may exist between certain physical hazards or the type of operation and the nature of post-operative complication. The most reliable figures are those that were obtained after elimination of all cases in which any type of physical disability had been present. In the remaining cases the surgical risk was minimized by the excellent condition of the patients, so that in this group the only known variable was the type of operation performed. Of these 1,497 patients there were 1,034 who had total hysterectomy and 463 who had subtotal hysterectomy.

EVALUATION OF THE TWO TYPES OF OPERATION

The basic reason for different opinions as to the best type of operation when hysterectomy

is considered is founded on the possible development of disease in the retained cervical stump subsequent to subtotal hysterectomy. It is true that in some hands few complications occur in the cervical stump after subtotal hysterectomy, whereas in other hands a long list of pathological changes takes place, making removal of the residual stump at the time of operation the procedure of choice. As to the occurrence of carcinoma in the retained cervical stump, we have little to add. During the 5 year period (1935 to 1939 inclusive) in which the two types of operation were performed in the groups cited, carcinoma of the cervix did not arise in any of the 764 cases in which subtotal hysterectomy was performed. Follow-up reports were not received from the patients during the 18 months previous to the writing of this paper and the future cannot be foretold, however, from insurance tables it is known that 25 per cent of deaths among women are due to carcinoma of the uterus. The ratio of carcinoma of the cervix to carcinoma of the uterus in cases treated at the Mayo Clinic is roughly 3:1. It is apparent that in all probability carcinoma will develop in the retained cervical stump in approximately 2 per cent of the cases in this group.

Black reported several groups of patients who had carcinoma of the cervix. From 21 per cent to 81 per cent of the carcinomas had developed in retained cervical stumps after subtotal hysterectomy. Although these figures do not afford a clue to the actual incidence of carcinoma arising in the stump, they do present forcefully the fact that malignant change occurs in the retained cervical stump subsequent to subtotal hysterectomy. Benign tumors so rarely arise in the cervical stump that the possibility of their development hardly justifies removal of the stump on this basis. Among 1,800 cases in which subtotal hysterectomy was performed Hays observed

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only 2 cases of benign tumors of the cervical stump following the operation.

Rosenow and Benedict (3) in work on certain types of intia, demonstrated definitely that the cervix is a persistent focus of infection. It has been shown also that a causal relationship exists between infection of the cervix and Hunner's ulcer. Although it cannot be stated that in every case of intia or of Hunner's ulcer the disease is due to an infected cervical stump it is known that this relationship can exist and that in certain cases remarkable cures have been obtained by excision of the infected cervix.

We believe that every patient presenting a diseased cervix in association with other uterine conditions requiring hysterectomy should have a total hysterectomy. This belief is based on the fact that 95 per cent of carcinomas of the cervix arise from erosion and chronic cervicitis. Cauterization of the cervix does not as a rule remove all gland-bearing tissue, nor does it remove the epithelium from the portio vaginalis which is frequently the primary focus of cervical cancer. Therefore, as a substitute for total hysterectomy application of cautery to cervix is a poor second.

Surgical results. To determine which type of operation was more satisfactory from the surgical standpoint we noted all of the cases in which surgical procedure on the cervix or in the vaginal vault was required subsequent to subtotal hysterectomy or to total hysterectomy. In 2 cases in which subtotal hysterectomy had been carried out prolapse developed which required excision of the cervical stump and a plastic vaginal operation. Prolapse of the vaginal vault did not occur in any case in the group in which total hysterectomy had been performed. The type of secondary procedure most commonly required on the cervical stump was the application of cautery for chronic cervicitis. The secondary procedure most commonly employed among the group in which total hysterectomy had been done was removal of a vaginal polyp. In most instances situated at the point where the vaginal wall was everted at the time of the primary surgical operation. In the group of patients mentioned earlier who presented the lowest surgical risk the incidence of secondary

surgical procedures after subtotal hysterectomy was almost twice as high as after total hysterectomy (Table I).

Among the 1,920 patients who had been subjected to total hysterectomy it was surprising that during the 5 year period of observation prolapse of the vaginal vault did not occur. Further to investigate this point we examined the records of all cases in which operation for vaginal prolapse had been performed during the same 5 year period (1935 to 1939 inclusive). In only 1 case had total hysterectomy been performed there were 23 cases of prolapsed cervical stump. The interesting point about these cases is that in the majority nearly 10 years elapsed between the original operation and the return for the secondary procedure. On this basis, vaginal prolapse among the group reported in this paper will not become evident for several years. This time element seems reasonable when the normal atrophy relaxation, and obesity that occur among most women from 40 to 60 years of age are considered. In 20 per cent of the cases of prolapsed cervical stump, the prolapse was evident before surgical intervention and recurred shortly afterward. The results in this small group emphasize the advisability of performing an associated vaginal plastic operation in such cases if relaxation is present at time the uterus is removed.

Postoperative complications. Among the group of patients who were excellent subjects for operation the complications were classified as follows: (1) postoperative intestinal obstruction, (2) postoperative hernias, (3) poorly healed wounds, (4) parotitis and (5) pulmonary complications. The incidence of each type of complication was about the same after total hysterectomy as after subtotal hysterectomy. There was not any statistically significant difference in incidence of these complications among 1,497 cases in which the only known variable was the type of hysterectomy performed.

The one outstanding exception to the incidence of postoperative complications was observed after total hysterectomy. In 8 cases of 1,034 in which total hysterectomy was performed there developed postoperative bleeding that required active treatment for control. In

TABLE I—INCIDENCE OF SECONDARY PROCEDURES CASES OF LEAST RISK

Procedure	Cases	Second operation required	Per cent
Total hysterectomy	1034	12	1.2
Subtotal hysterectomy	463	11	2.38
Total	1497	23	1.5

practically every case the bleeding was from the everted vaginal mucosa. In the 463 cases in which subtotal hysterectomy was performed postoperative hemorrhage did not take place. The vaginal wall is not cut in carrying out subtotal hysterectomy, consequently, the possibility of hemorrhage from this site does not arise.

In a previous paper (4) we stated that the incidence of pulmonary emboli is higher after subtotal hysterectomy than after total hysterectomy. The explanation of this difference probably is related to the engorgement of the lymphatic channels from the retained cervical stump and to the associated secondary thrombosis in the veins of the broad ligament. Similarly, we demonstrated (4) that the incidence of thrombophlebitis is higher after subtotal than after total hysterectomy.

On the other hand we showed (4) that the incidence of urinary complications following total hysterectomy is higher than that following subtotal hysterectomy. This variation is due to the fact that the dissection of the bladder required in total hysterectomy is wider than in subtotal hysterectomy and therefore causes greater trauma and possibly more damage to sympathetic nerve fibers, resulting in temporary urinary retention which necessitates catheterization for relief. The incidence of vesical infection is parallel to the number of catheterizations, and consequently is higher after total hysterectomy than after the subtotal procedure.

In an earlier paper we demonstrated (4) that the mortality rate in the presence of pelvic infection following total hysterectomy is much higher than following subtotal hysterectomy. The reason for this apparent fact is not definitely known.

Type of convalescence. Much has been said regarding convalescence after total or subtotal hysterectomy. The question of which type of operation carries the least postopera-

TABLE II—DIFFERENCE IN MORTALITY RATES ENTIRE GROUP

Procedure	Cases	Hospital deaths	Per cent
Total hysterectomy	1920	15	0.78
Subtotal hysterectomy	764	8	1.04
Entire group	2684	23	0.85

tive reaction has been argued in both directions. In order to satisfy our own minds on these points we selected 458 consecutive uncomplicated cases in which hysterectomy had been performed during a single year. Three hundred and forty-eight of the patients had total hysterectomy and 110 had subtotal hysterectomy. In each case record was kept as to (1) the highest peak of fever reached postoperatively, (2) the number of days the temperature remained at 100 degrees F (37.8° C) or was higher, and (3) the length of the patient's stay in the hospital. In each regard there was a slight, though definite, difference in favor of subtotal hysterectomy. For any given number of the patients who had total hysterectomy, the fever reached a peak from 0.5 to 0.75 degrees F higher than for the same number who had subtotal hysterectomy. In regard to the duration of fever higher than 100 degrees F (37.8° C) recordings in comparable groups revealed that in the cases in which total hysterectomy was done there was roughly a half day more of fever than when subtotal hysterectomy was performed. The postoperative stay in hospital was a third of a day longer for patients who had total hysterectomy than for those who had subtotal.

The number of cases here presented seems adequate to afford a definite deduction as to the postoperative reaction of patients to these two types of operation. Beyond question, in comparable cases the operation of total abdominal hysterectomy is associated with a sharper and more prolonged reaction than is subtotal hysterectomy.

Mortality. The foregoing statement suggests that the mortality rate should be higher in the group of patients who are subjected to total hysterectomy. An analysis of the hospital deaths, however, does not substantiate this assumption. Table II demonstrates that the mortality rate following total hysterectomy is 0.26 per cent lower than that following

TABLE III.—DIFFERENCE IN MORTALITY RATES CASES OF LEAST RISK

Procedure	Cases	Hospital deaths	Per cent
Total hysterectomy	34		8
Subtotal hysterectomy	493	4	86

subtotal hysterectomy. This figure takes on more significance when it is seen that the mortality rate for the entire group is only 0.85 per cent. When only the patients who were excellent subjects for operation are considered, the difference is even more pronounced. Table III indicated a mortality rate 0.68 per cent lower for the group in which total hysterectomy was performed.

Peritonitis remains the cause of death most commonly encountered. Thirteen of the 23 hospital deaths were due to this complication. Four deaths were caused by pulmonary emboli, 2 by bronchopneumonia and 1 each by (1) acute nephritis, (2) shock (3) atelectasis, and (4) postoperative hemorrhage.

Nine of the 13 deaths from peritonitis occurred in the group of patients who had total hysterectomy. The remaining 4 followed subtotal hysterectomy. The incidence was practically the same for the two types of procedure, 9 in 1,920, or 0.46 per cent, for the former type and 4 in 764, or 0.52 per cent for the latter.

From these figures it would seem that neither operation offers a difference in the possibility of subsequent development of fatal peritonitis. However as we demonstrated previously among those patients who present evidence of infection at the time of surgical intervention the mortality rate is definitely higher following total hysterectomy than following subtotal hysterectomy. For this group of patients, therefore the operation of choice is subtotal hysterectomy.

SUMMARY

In a review of 2,684 consecutive cases in which abdominal hysterectomy was performed for benign conditions, analysis was made of the postoperative complications and of the results obtained. Of the 2,684 patients, 1,920

were subjected to total hysterectomy and 764 to subtotal hysterectomy.

Total abdominal hysterectomy is favored by the following considerations: (1) The cervix as a possible source of subsequent malignant change is eliminated. (2) The cervix as a focus of infection is removed completely. (3) A more stable vaginal vault is obtained and secondary operations are obviated. (4) The incidence of postoperative pulmonary emboli and postoperative thrombophlebitis is lower. (5) The mortality rate is lower.

Subtotal hysterectomy also is favored by various considerations: (1) The postoperative reaction of the patient is less marked. (2) The incidence of urinary complication is lower. (3) There is not any danger of secondary hemorrhage from the vaginal vault. (4) In cases in which infection is present at the time of surgical intervention the mortality rate is lower.

CONCLUSIONS

Comparison of the postoperative complications and the results in the two groups of cases furnished the basis for our conclusions:

1. The elimination of the cervix as a source of subsequent trouble and the lower mortality rate associated with its removal far outweigh any known complication that may arise after total abdominal hysterectomy.

2. Except for cases in which infection is present at the time of operation total hysterectomy apparently is the operation of choice when surgical removal of the uterus for benign conditions is indicated.

3. The secondary hemorrhage from the vaginal vault and the increased urinary complications which follow total hysterectomy usually respond satisfactorily to appropriate treatment.

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A STUDY OF THE MECHANICS OF BILE FLOW

III Responses to Pharmacological Stimuli

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IN an earlier paper (12) we have described the method of simultaneously observing the effects of those structures we considered most important in controlling the flow of bile. In that communication we also reported our observations on the influence of physiological intravenous solutions upon these structures. In a subsequent report (13) we described the effects of instillation of various solutions into the duodenum. In the present paper we wish to present the results of stimulating the gall bladder, sphincter of Oddi, and the duodenum with pharmacological agents introduced intravenously. The experimental technique is identical to that used in the two reports mentioned.

Adrenalin was injected intravenously fourteen times into 12 dogs, 0.1 cubic centimeter of a 1:1000 solution was the usual dose. The variability in the response of the gall bladder to adrenalin has been recognized in the literature and our results on the effect of adrenalin on the sphincter and duodenum, in addition, illustrate a similar variable effect. In a number of animals the response of the sphincter was diphasic, i.e., an initial decrease of its tone was followed by a secondary rise. In the duodenum the effect was one of a transitory inhibition of activity and decrease in tonus, followed by a rise in tonus and motility concomitant to the secondary rise in sphincteric resistance. The degree of response varied among different dogs, and in some the only effect seen was the rise in sphincteric and duodenal tone. In the latter group the gall bladder showed a relaxation but no change in motility. In one animal the drop in sphincteric resistance far exceeded the subsequent rise above normal and at the same time the gall

bladder contracted instead of relaxing as was more commonly observed. Lueth (15) has drawn attention to the fact that the effect of adrenalin on the sphincter varies with dosage.

The use of another member of the adrenalin group, epinine (0.2 c.c. of a 1:100 solution intravenously) gave similar variable results (Fig. 3). With this latter drug the gall bladder showed contractions more frequently than with adrenalin. Ephedrine gave responses in no respect different from those of adrenalin and epinine.

Propradrine hydrochloride injected intravenously in 20 milligram doses gave similar but less marked results in the individual animal. The characteristic rise in blood pressure following intravenous injections of medium doses of adrenalin and epinine was usually followed by a subsequent drop below normal, this secondary drop was absent in the case of ephedrine and propradrine.

The effect of adrenalin was diminished but not abolished by a previous injection of trasentin or of atropine. It may be of significance that the same animal usually responded in a uniform manner to any of these adrenergic drugs used. This would imply that another explanation of the variable responses to injections of sympathomimetic drugs may lie in the individual response to stimulation of the autonomic system.

Houssay and Rubio found that the sympathomimetic drugs relaxed the isolated, perfused gall bladder, adrenalin being more effective than ephedrine. After atropine, these drugs still had the same effect. Other literature is quite contradictory. Some (1) describe contraction of the gall bladder on direct application of adrenalin. Some describe a diphasic (1) or triphasic (27) response with large intravenous doses. Necheles found contraction of the gall bladder in normal unanesthetized dogs (19).

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A preliminary report was read at the meetings of the American Physiological Society, April 19, 1941, Chicago.

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Fig. 1. At 1 prostigmine, given intravenously produced an initial simultaneous spasm of the sphincter and duodenum. Subsequently duodenal tone rose steadily while sphincter tone remained practically normal. At 25 and 26 repeated intravenous doses of acetylcholine, produced slight immediate effects. Thereafter, diphasic relaxation and contractions of the sphincter occurred, independent of unsustained tonic contraction of the duodenum. At 3, papaverine, 1 showed simultaneous rise in the tone of the sphincter and duodenum, however the sphincter relaxed while elevated duodenal tone persisted. The gall bladder showed an immediate small relaxation. Codeine produced simultaneous immediate spasm of sphincter and duodenum.

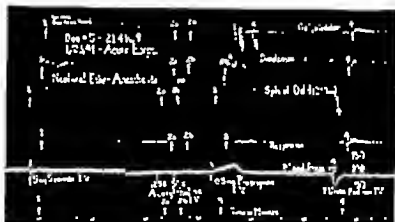


Fig. 2. At 1 acetylcholine preparation, 1 produced marked tonic contraction of the gall bladder which persisted for approximately 30 minutes. An increase in duodenal tone and motility occurred simultaneously, but sphincter pressure was hardly affected. At 25 and 26, atropine, given intravenously produced relatively small changes in duodenum and sphincter. At 3, intravenous prostigmine, produced marked recurring simultaneous spasms of sphincter and duodenum. Gall bladder showed only respiratory effect. At 4, units of padutin produced moderate spasm of sphincter no particular change in duodenum, and small contraction of the gall bladder.

Acetylcholine was injected in 5 animals in doses varying from 5 to 50 gamma intravenously. In only one instance was there a significant effect. In this case there was a marked lowering of intraductal pressure associated with recurrent episodes of duodenal spasm. The gall bladder showed no response. In all

other cases the response was relatively insignificant, except when a dose as large as 50 gamma was given. However when the injection of acetylcholine was preceded by prostigmine (Fig. 1) it was usually effective in eliciting moderate rises in intraductal pressure and duodenal motility. Loeth (15) described in-

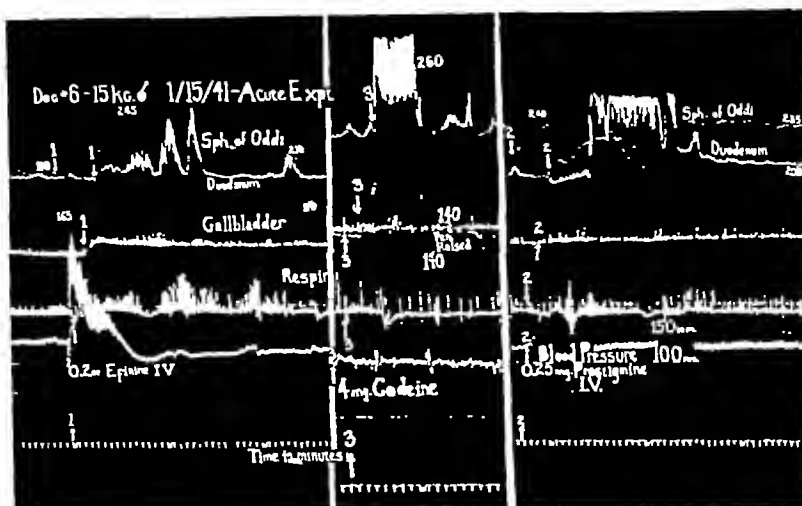


Fig 3 At 1, a recurrent diphasic response of the sphincter of epinine given intravenously, was seen. Note, that a fall of sphincter pressure was followed by a rise above normal. An elevated sphincter pressure persisted even when the duodenum had relaxed from its recurrent spastic contractions. The gall bladder showed a marked prolonged tonic contraction. This animal responded in a similar manner to adrenalin and propantholone. At 2, intravenous prostigmine, produced several recurring sphincter spasms which preceded and persisted long after the duodenum had relaxed from a prolonged spasm. Gall bladder showed no significant changes. At 3, intravenous codeine, produced a marked immediate spasm of sphincter and duodenum. No effect on gall bladder.

creases in sphincter pressure and duodenal tone due to acetylcholine. Sandbloom, Voetglin, and Ivy attribute any gall-bladder contractions with this drug to changes in liver volume.

Prostigmine in 0.2 to 0.25 milligram doses intravenously was effective in every case of 12 animals in producing a marked sphincteric and duodenal spasm and usually no effect on the gall bladder (Figs 1 and 3). Under the influence of prostigmine, we have frequently seen the sphincter relax in the midst of a prolonged duodenal spasm, and vice versa (Figs 1 and 3). We have had occasion to refer to this independent activity of these two structures under other conditions in our previous publications (12, 13). No significant increase in the tonus or motility of the gall bladder was observed. In one atropinized animal prostigmine was completely without effect (Fig 4). Our results with this drug are compatible with the reports of others using physostigmine (3, 5, 14).

Pilocarpine 0.5 to 1 milligram intravenously, produced marked gall-bladder contractions

and a simultaneous rise in sphincteric pressure and duodenal tone in every one of the 8 cases in which it was used (Fig 6). A 25 milligram dose of trasentin abruptly abolished the tonic contraction of the gall bladder produced by pilocarpine in one dog. The ability of pilocarpine to contract the gall bladder is generally recognized (3, 11, 14, 22, 27, 29), but its inability to evacuate the gall bladder is attributed to the sphincteric spasm which occurs at the same time (5, 9, 29).

Five milligrams of a secretin-cholecystokin preparation was injected intravenously 8 times in 7 animals. In each instance an immediate tonic contraction of the gall bladder and duodenum followed (Fig 2). This is in agreement with previous work (2, 8, 10, 26). After an interval of several minutes an increase in sphincteric resistance occurred, during this interval we believe effective gall-bladder evacuation can occur (Fig 2). The tonic contraction of the gall bladder was considerable and persisted for 20 or more minutes, long after duodenal or sphincter spasm had subsided. The dose of secretin-cholecys-

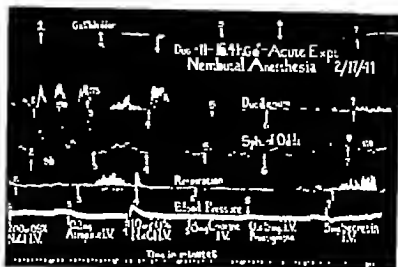


Fig. 4. The effect of tropics on spasm producing agents. At normal saline, gives intravenously produced recurrent increases in sphincter tone, concurrent with duodenal activity. At 3, intravenous atropine, inhibited both of these responses. At 4, intravenous hypertonic saline, produced its usual spastic effect on the sphincter and duodenum. At 5, intravenous cocaine, was completely without its usual effect. At 6, intravenous strychnine, as likewise ineffective. At 7, secretin-cholecystokin preparation produced marked tonic contraction of the gall bladder without duodenal and sphincter response probably due to the atropinisation.

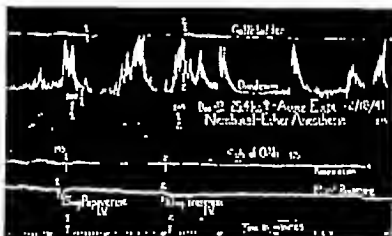


Fig. 5. At intravenous papaverine produced precipitous drop in sphincter pressure previously produced by normal saline, its gradual return to previous levels. The duodenum was inhibited and the gall bladder relaxed sooner but. At intravenous trasentin was followed by an immediate drop in sphincter pressure while duodenal tone and motility were at first unaffected. Gall-bladder tone dropped slightly. The sphincter pressure was maintained at low level, while later duodenal activity was inhibited for shorter period of time. Gradually there was return to previous state of activity.

tokinin used had no significant effect upon blood pressure. Previous administration of atropine or trasentin had little or no influence on the effects of this drug (Figs. 4 and 6).

The response of the sphincter and duodenum to papaverine in 8 to 15 milligram doses, intravenously, showed considerable variation. In 5 of 10 cases there was an initial relaxation followed by a subsequent rise to or above normal (Fig 5), in others, spasm of sphincter and duodenum were a dominant effect (Fig 1). In every instance that papaverine had an effect on the gall bladder, it was one of moderate relaxation (Figs 1 and 5). Papaverine produced relaxation of a tonic contraction of the gall bladder produced by cholecystokinin in 2 dogs. This relaxing effect of papaverine on the gall bladder has been observed by others (9, 18).

Four to 8 milligrams of codeine produced marked increases in sphincteric tone and duodenal peristalsis in every case in which it was employed (Figs 1 and 3). The effect was immediate and did not appear to influence the gall bladder. Previous injections of atropine and traserutin reduced or abolished the effect of codeine (Figs 4 and 6). The literature is replete with accounts of the spastic effect of opiates on all smooth muscle (7, 23, 24). Although no specific information is available on the influence of codeine on the gall bladder, a closely related alkaloid morphine is thought to be without really significant effect (8, 14, 17, 27).

Atropine, 0.2 to 0.3 milligram intravenously abolished the tonus rhythm of the sphincter as well as duodenal motility. The depressant action of atropine on intestinal activity is well known (6, 15, 24). The small doses employed of this drug did not actually lower intramural pressure, but rather inhibited the occurrence of spasms. The same doses of the drug were without effect on the gall bladder other than a slight decrease in tonus rhythm.

Various agents, of known ability to produce spasms of the sphincter and duodenum, were given after atropinization with the following results. Atropine was ineffective in abolishing the spasm of the sphincter and duodenum produced by gastric juice introduced into the duodenum, of intravenous adrenalin, and of intravenous hypertonic saline (Fig 4). The effect of prostigmine (Fig 4) and of normal saline intravenously (Fig 4) was abolished and the effect of codeine (Fig 4) was either

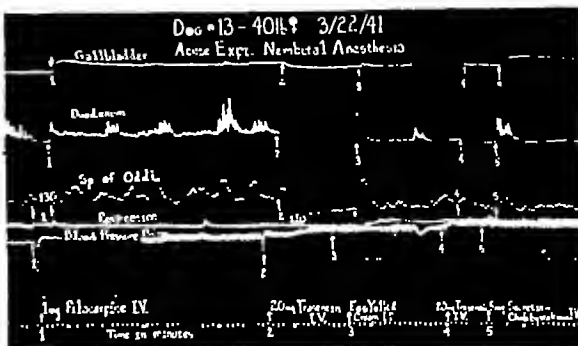


Fig 6 At 1, intravenous pilocarpine produced an immediate tonic contraction of the gall bladder of about 20 minutes duration. Simultaneously a moderate increase in the tonus of the duodenum ensued with a similar response of the sphincter after more of an interval than is usual. At 2, intravenous traserutin, a synthetic antispasmodic, produced a significant relaxation of all three structures. Intraduodenal instillation of a mixture of egg yolk and cream at 3 produces a contraction of all three structures despite the previous antispasmodic medication. Likewise, another injection of traserutin at 4, did not influence the effect of a secretin-cholecystokinin preparation injected intravenously at 5.

reduced or completely inhibited. Secretin was capable of producing a moderate gall-bladder contraction following atropinization. Ivy (9) reported that the effect of cholecystokinin on the gall bladder was not prevented by atropine. We were not able to confirm the relaxation of the gall bladder with atropine noted by many workers (9, 10, 11, 14, 16), although we occasionally saw a decreased tonus rhythm, however, we used relatively small doses of atropine.

Traserutin A had similar effects as atropine, in doses of 10 to 25 milligrams intravenously (Figs 5 and 6). As with atropine, the effects of adrenergic drugs were not influenced, nor was hypertonic saline, intraduodenal instillation of gastric juice, or egg yolk, or secretin-cholecystokinin. Traserutin relaxed a tonic contraction of the gall bladder induced by pilocarpine in one dog. The new traserutin A preparation which was used did not seem to have such pronounced effects on relaxation of the gall bladder as traserutin was reported to have had (21).

Pituitrin was administered intravenously to 3 animals, and in all 3 a moderate gall-bladder contraction occurred before a moderate rise in sphincter pressure and duodenal spasm, the latter followed after an interval of several

minutes. The contraction of the gall bladder following intravenous surgical pituitrin does not compare with that produced by cholecystokinin or pilocarpine. An initial decrease preceding the rise of tone of the sphincter and duodenum described by some (5-15) was not seen. Gall bladder contraction with pituitrin has been described by others (8).

Decholin 0.5 to 1 cubic centimeter was injected intravenously into 4 dogs, with varying results. There was no characteristic response of the sphincter or duodenum, but the gall bladder relaxed in 3 of the 4 animals used. The use of this drug was associated with a marked increase—about 50 per cent.—in the flow of bile collected from the hepatic ducts.

A urinary extract with vasodilator properties *padutin*, was investigated. The drug had variable effects on the sphincter and duodenum in a normal state of tone but appeared to relieve a state of spasm of the sphincter produced by other measures.

Nitroglycerin and amyl nitrite also produced temporary relaxation of the sphincter from a spastic state. Theophylline had no significant effects.

Experiments on human subjects. Patients that had been subjected to cholecystectomy and common duct drainage were utilized after biliary drainage had been established and the patient recovered from the operation. Similar to the procedure of Doubilet and Colp and Walters et al the common duct was perfused with saline solution and connected to an oil-carbon tetrachloride manometer which accurately indicated the resistance of the sphincter of Oddi to the flow of perfusion. Various drugs were administered by injection, orally or admixed to the perfusion fluid. It is beyond the scope and extent of this paper to discuss these results in detail, and they will be reported separately (20) but it may be stated that a number of observations on the dog reported, were corroborated on the human.

ANALYSIS OF STUDY

The most important factor in the emptying of the gall bladder ought to be that of reciprocal innervation of the gall bladder on the one side and sphincter and duodenum on the other. This process has been described as

contraction of the gall bladder with simultaneous relaxation of the sphincter of Oddi and duodenum. Whether such a reflex exists or not, it is apparent that emptying of the gall bladder can occur only if during contraction of this organ the sphincter and duodenum do not remain contracted all the time. In other words if there is no orderly reciprocal innervation there must be at least temporary periods of relaxation of sphincter and duodenum during contractions of the gall bladder in order to permit a more or less effective emptying of that organ. We have analyzed these possibilities in our experiments and therefore can answer the above question. The gall bladder may empty either by reciprocal innervation or by contraction of the gall bladder during temporary relaxation of both sphincter and duodenum either waves of duodenal contractions pass over the sphincter leaving it open during the intervals between waves, or the rhythmic opening and closing of the sphincter continues and emptying occurs in these animals with a more or less quiet duodenum or third, both of these possibilities are combined. The occurrence of these combinations can be studied from the illustrations. For instance in Figures 2-4 and 6 following the administration of secretin-cholecystokinin, a marked gall-bladder contraction occurred, which persisted for 30 or more minutes. Although waves of moderate duodenal contraction are immediately induced, sphincter pressure remains low enough for a long enough interval against which the gall bladder could effectively evacuate.

The experiments here reported demonstrate that emptying of bile through the sphincter of Oddi and the emptying mechanism of the gall bladder depend on a number of processes, the timing and intensity of which are the determining factors. It is also demonstrated that reciprocal innervation of gall bladder and of the duodenum and sphincter of Oddi may occur but it is not a necessary assumption for the emptying reflex of the gall bladder. It is further evident that a combination of drugs may offer great possibilities for the eventual substitution of the fat meal usually employed in cholecystography. Experiments to answer this question are in progress.

SUMMARY

- 1 The response of the sphincter of Oddi to drug stimulation can be independent of duodenal activity
- 2 The emptying mechanism of the gall bladder and the flow of bile through the sphincter of Oddi depend upon a number of processes, the timing and intensity of which are the determining factors
- 3 Reciprocal innervation of the gall bladder, the sphincter of Oddi, and the duodenum may possibly occur, but it is not a necessary assumption for the emptying reflex of the gall bladder
- 4 Adrenergic drugs which were employed in this study consisted of epinephrine, epinine, ephedrine, and propradrine, all members of this series produced such variable results that they appeared to offer little clinical application
- 5 Cholinergic drugs employed were acetylcholine, prostigmine, and pilocarpine. All of these produce contractions of the sphincter and duodenum, of varying degree, and also contractions of the gall bladder in the case of pilocarpine
- 6 Codeine produced subtetanic contractions of the sphincter of Oddi and the duodenum without affecting the gall bladder
- 7 Secretin-cholecystokinin produced the most effective contractions for evacuation of the gall bladder, but no reciprocal mechanism was evident
- 8 The most effective spasmolytic drugs in our hands were found to be atropine and traseratin
- 9 The possibility of a combination of drugs which would produce effective gall-bladder evacuation against a relaxed sphincter of Oddi is suggested as an eventual substitute for the fat meal usually employed in cholecystography

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Fig 1 The lumen is dilated throughout. Mucosal and submucosal layers show atrophy.¹

6, appendices showing no evidence of obstruction

Group 1 presents a uniformly dilated lumen (Fig 1) from the proximal end to the tip. The changes in the mucosa and submucosa were variable. In some these were quite marked, showing thinning, diminution in number and length of glands with loss of submucosal lymphoid tissue. The muscle layers were thinned. In specimens in which atrophy of the layers was present, the mucosa always presented the most marked change.

In other specimens the wall was thick with hyperplastic lymph follicles having an oblong shape, the long axis being parallel with the circumference of the lumen (Fig 2).

In Group 2 the proximal segments were dilated. Then there was a variable sized lumen to the tip. This variation usually occurred in the midthird (Fig 3). The lumen was small, slit-like, the mucosa appearing normal and the lymphoid tissue abundant.

¹The photographs are mounted so that the upper left segment is the base of the appendix and the lower right segment is the tip.



Fig 3 The lumen is dilated in the 2 proximal segments, slit like in the third and fourth segments, and increasingly distended in the fifth, sixth, seventh, and eighth segments. Lymphoid hyperplasia is present throughout.

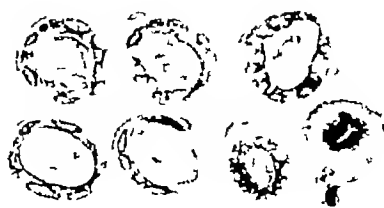


Fig 2 The lumen is dilated throughout the first 5 segments. There is hyperplasia of the lymphoid tissue. The germinal centers are elongated, their long axis parallel to the circumference of the lumen.

Then two or three sections might be encountered with areas of luminal dilatation and mucosal thinning.

Group 3 showed evidence of a variable sized lumen along the appendix (Fig 4). The first segments showed a narrow lumen. Then the lumen was uniformly dilated to the tip, or it would show several points of narrowing with interdilatation.

Group 4 showed a uniformly small lumen (Fig 5) with the submucosa markedly thickened due to a large amount of fibrous tissue in the submucosa. The mucosal glands, although decreased in number, were normal in size.

Group 5 showed partial or complete obliteration of the lumen (Fig 6). The primary change was replacement of mucosa and submucosa by a fibrous core, and one showed a neurofibroma. No conclusive evidence of pre-existing inflammation was seen.

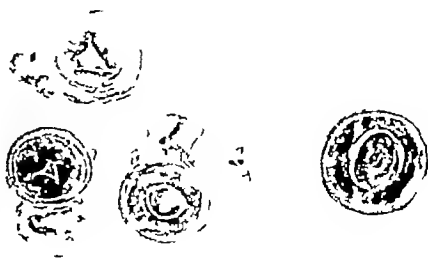


Fig 4 The lumen is small in the 2 proximal segments with a markedly thickened wall. There is distention in the 2 distal segments. Abundant lymphoid tissue is present in the 3 terminal segments.



Fig. 5. The lumen is narrow throughout, slit like in the third segment. The wall is greatly thickened due to the increase in fibrous tissue in the submucosa.



Fig. 6. The lumen is replaced by fibrous core except in the proximal segment.

Group 6 showed no structural variations from the normal.

When the lumen was dilated either uniformly or irregularly with definite atrophic changes in the layers of the wall (groups 1, 2 and 3) it was thought that these changes were caused by accumulation of fecal material in the lumen with resultant increased intraluminary pressure, this accumulation being due to obstruction or atony of the appendix.

Group 4 showed no atrophic changes but did show a marked variation in the lumen, sufficient to obstruct partially the interchange of fecal material with the caecum.

The appearance of group 5 suggested that it might be an early phase of obliteration of the lumen as seen in group 6.

Groups 2 and 3 show histological evidence of partial obstruction in the wall due to focal lymphoid hyperplasia. We are uncertain whether this is a primary state or whether acute kinks, due to congenital bands, might have prevented the lumen from distending at these points thus preventing any pressure changes from intraluminary pressure.

Group 1 showed no site of obstruction but definite evidence of increased intraluminary pressure. It was believed that an obstruction could occur at the appendiceocecal junction since the appendix enters the cecum at an acute angle in most cases. When the angle is acute the mucosal fold at the opening (valve of Gerlach) is more prominent.

In these sections it was noted that in specimens in which the lumen was dilated if lymphoid follicles were present they were oblong in shape and the long axis of the

follicle was parallel to the circumference of the lumen. This was not true if the lumen was not dilated.

Comparing these groups, obstruction occurred in 18 of 28 or 64 per cent, noninflamed specimens removed surgically in 36 of 52 or 69 per cent, inflamed specimens removed surgically and in 15 of 49 or 30.6 per cent specimens removed at autopsy.

In groups 1, 2 and 3 of the noninflamed specimens we believe that dilatation of the proximal segments indicates obstruction at the appendiceocecal junction. When there was evidence of obstruction along the appendix at one or more points, the structural variation was a comparative one. While the lymphoid tissue was comparatively abundant and hyperplastic in relation to adjacent dilated segments, actually the mucosa and lymphoid tissue in many cases were normal. We therefore, believed that extrinsic bands with acute kinks rather than true focal lymphoid hyperplasia may have been responsible for this picture.

We are not prepared to say whether lymphoid hyperplasia *per se* may produce appendiceal obstruction.

By this method of pathological examination we are of the opinion that the pathologist can make a diagnosis of appendiceal obstruction.

The third group of appendices studied consisted of 25 appendiceocecal regions removed from stillborn infants and newborn babies which had died. A representative group is shown in drawings (Fig. 7) illustrating the marked variations in position and the presence

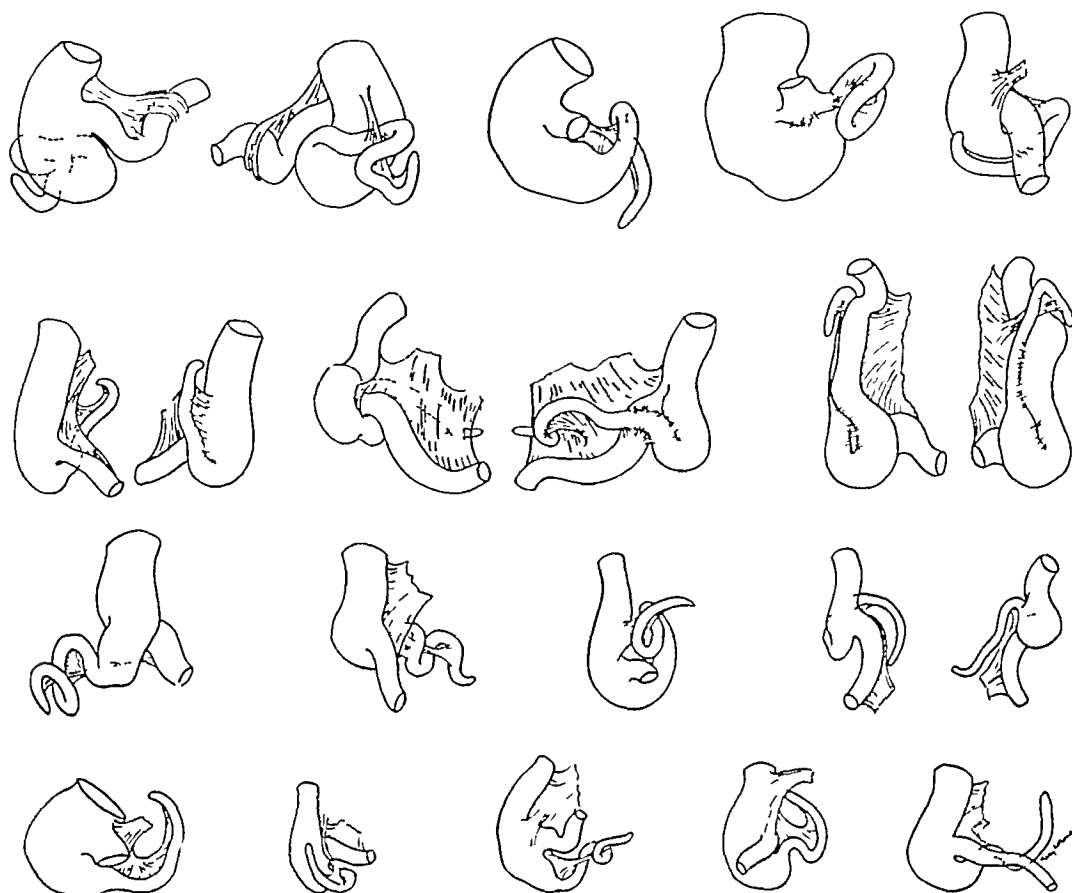


Fig 7 Drawing of 16 consecutive specimens removed at necropsy Numbers 1, 5, 6, 7, and 11 show both an anterior and posterior view

of numerous congenital bands causing distortion of the appendix. The appendix was free of bands in only 7 cases. The variations seen here represent almost every type encountered surgically and are presented to emphasize the extreme distortion at birth.

The role of obstruction in the etiology of acute appendicitis has long been recognized (5, 7, 11, 12, 13, 14, 15, 16). However, when one peruses the literature on "chronic appendicitis," evaluation becomes extremely difficult because there is no uniform classification which is followed by the clinician and the pathologist.

The term "chronic appendicitis" as generally used has ceased to be a disease entity but rather a 'catch all' for those cases not showing active inflammation.

In the pathological department at Bellevue Hospital the following classification has been used:

1. Inflammatory
 - acute
 - chronic
 - nonspecific
 - specific
2. Non-inflammatory
 - obstructed with
 - lymphoid hyperplasia
 - sclerosis
 - atrophy etc
 - nonobstructed
 - lymphoid hyperplasia
 - sclerosis
 - atrophy etc
3. Neoplastic
 - benign
 - carcinoid
 - neurofibroma etc
 - malignant—carcinoma etc

The term chronic appendicitis is used only when signs of active chronic inflammation are

present. This represents less than 5 per cent of all appendices examined.

Many explanations have been given for the cause of pain in the noninflamed appendix. Barrs, in 1918 reported 7 cases of appendiceal disease in children all cured by appendectomy in which the pathological diagnosis was lymphoid hyperplasia.

Symmers reported 20 cases with similar pathological changes and symptoms simulating those of mild appendicitis with cures following appendectomy.

Follow up records show that between 50 and 80 per cent of the patients in this general group operated upon are cured or markedly improved yet both surgeon and pathologist have been unable to distinguish the offending appendices from those which did not give symptoms.

Since histological evidence of disease is lacking one is forced to turn to disturbances in function for an explanation of the symptoms.

In *Human Physiology* by Flint, 1892 this statement appears: "The function of the appendix is unknown." Certain recent physiological textbooks fail to mention the organ. Dufor (10) in 1890 advanced the theory that the appendix plays a great part in provoking a desire for defecation independent of other reflexes involved in the act. Adams and McCrae (10) in 1914 stated: "It is the appendix that is the hydrostatic agent initiating peristalsis in the large gut." These views have not been widely accepted and Flint's statement still stands. "The function of the appendix is unknown."

Although no useful function has been established, we do know that it functions as part of the large bowel that it is capable of filling and emptying and that the peristaltic action is similar to that of the large bowel (13).

Anatomically the appendix vermiformis must be considered as an undeveloped cecum. Embryologically the appendix is a retrogressive organ having a relatively higher development in the fetus than in the infant, and must be considered merely as the distal portion of the cecum (7).

Differentiation between cecum and appendix starts about the seventh week and con-

tinues to birth when the comparative diameters are 1:4 at 8 years it is 1:6 or 7 and in the adult the ratio is 1:8 or more. One would, therefore, consider comparative retrogression not complete until puberty (7).

The relative location of the appendix is the most variable of any organ in the peritoneal cavity. The location depends on the point of origin from the cecum and varies, first according to the direction of the cecal pouch, and second according to the presence of peritoneal bands which permit following complete rotation of the large bowel.

The appendix is found free of congenital peritoneal bands and entering the cecum at a right angle in about one-third of the cases. The angle at which the appendix enters the cecum varies between 10 and 90 degrees.

The clinical syndrome with which the obstructed appendix is associated is well known. Pain in the right lower quadrant is the one constant symptom steady or intermittent, frequently associated with anorexia, nausea, and occasional vomiting. The patients are frequently constipated. The only constant sign is tenderness in the right lower quadrant centering over McBurney's point usually associated with skin hyperesthesia (8). Evidence of active inflammation is lacking. The temperature is normal and the blood count not elevated.

Can the appendix give these symptoms and signs without showing any evidence of inflammation? We believe it can, and does.

It has been shown (8) that distention of the lumen of a normal appendix will give epigastric pain, nausea and pain in the right lower quadrant associated with persistent skin hyperesthesia. This was done through appendicostomies. Therefore it is reasonable to assume that increased intraluminal pressure due to natural causes can give the same clinical symptoms and signs.

The appendix is a tube, blind at one end and lined with intestinal mucosa capable of secretion and absorption. It opens into the cecum. Intestinal contents reach the cecum in a fluid state, some entering the appendix. Dehydration occurs, and any variation in the diameter of the lumen will fix or stasis and accumulation of fecal material. This process

we believe, will cause distention of the lumen with resultant changes in the mucosa which can be demonstrated histologically by the method of examination herein described.

Anatomically, three methods of obstruction are possible: (1) kinking at the appendicocolic junction, (2) kinking along the length of the appendix due to peritoneal bands, and (3) intra-appendiceal stenosis due to lymphoid hyperplasia or fibrosis.

The point of origin of the appendix from the cecum varies according to the direction of the cecal pouch, and the appendicocolic angle is dependent on the position and development of the peritoneal bands which, in turn, depend on the ultimate position of the large bowel.

Intrinsic obstruction occurs due to variations in the thickness and structure of the wall with consequent encroachment on the lumen.

The first two causes of obstruction, namely, an acute appendicocolic angle and kinking due to peritoneal bands, will be seen only by the surgeon, and in writing up the operation, these details are frequently omitted. Consequently, this information does not reach the pathologist. However, the third cause, namely, intrinsic obstruction, can be seen by the pathologist, but unless the specimen is studied carefully, evidence for intrinsic obstruction may not be recognized.

SUMMARY AND CONCLUSIONS

1. Histological criteria for diagnosing appendiceal obstruction are submitted.

2. Appendiceal obstruction was demonstrated in 18 of 28, or 64 per cent, noninflamed specimens removed surgically, in 36 of 52, or 69 per cent, inflamed specimens removed sur-

gically, and in 15 of 49, or 30.6 per cent specimens removed at autopsy.

3. This obstruction is believed to be mechanical rather than inflammatory. The etiological factors for obstruction are present at birth.

4. An obstructed appendix may give symptoms without the presence of inflammation.

5. An obstructed appendix definitely predisposes to acute appendicitis.

6. Appendiceal obstruction may exist without giving signs or symptoms.

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SUBACUTE STREPTOCOCCUS VIRIDANS SEPTICEMIA CURED BY EXCISION OF AN INFECTED TRAUMATIC ARTERIOVENOUS ANEURYSM

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THE rarity of coexisting acquired arteriovenous aneurysm and subacute *Streptococcus viridans* septicemia, is indicated by the fact that up to the present time only 10 such cases have been recorded in the literature. For purposes of classification they may be divided into two main groups.

The first group consists of cases in which the septicemia precedes, and is responsible for the formation of the aneurysm. Such a sequence sometimes is observed in subacute bacterial endocarditis, of which mycotic arteriovenous aneurysm may be a late complication. Cases have been reported by Masbrenier, Simmonds, Libman and Floyd.

The second group consists of cases in which arteriovenous aneurysm is the primary condition and subacute bacterial septicemia the complication. Primary arteriovenous aneurysms (and fistulas) may be either congenital or acquired. Among the better known congenital arteriovenous communications (fistulas) may be mentioned patent ductus arteriosus, patent interauricular septum, and patent interventricular septum. Acquired primary arteriovenous communications (aneurysms) are exclusively traumatic in origin and most commonly are due to gunshot or stab wounds.

Should a patient with an arteriovenous communication of either the congenital or acquired variety develop a transient bacteremia from some extraneous source organisms may lodge upon the intimal lining of the arteriovenous lesion. Under such circumstances, vegetations may develop locally, thus there is established a new infective focus from which organisms are shed into the blood

stream more or less continuously. When these organisms are of low virulence the patient suffers from a condition termed subacute bacterial septicemia." The organism most commonly involved in the latter is the *Streptococcus viridans*.

The frequency with which subacute *Streptococcus viridans* infection develops at the site of congenital arteriovenous communications, especially those located within the heart is well known and many such cases have been collected by Abbott. The superimposition of similar infection upon acquired arteriovenous communications (aneurysms) although observed less commonly has been reported by Bretschneider, Wala, Gravier, Porter and Williams, Hamman and Rlenhoff and Leaman. When subacute *Streptococcus viridans* infection develops at the site of an acquired or congenital arteriovenous communication and organisms continue to be shed into the blood stream, new infective lesions may develop at distant points. One of the most common sites for such secondary localization is upon the endocardium and cardiac valves. When this occurs, the fresh cardiac lesions constitute additional infective foci which themselves are capable of perpetuating the sepsis.

Although arteriovenous communication existing in combination with subacute *Streptococcus viridans* septicemia formerly was considered to be of interest only to the pathologist and internist it recently has attracted the attention of the surgeon also. This interest was initiated in 1935 by the report of Hamman and Rlenhoff of the first case in which cure of subacute *Streptococcus viridans* septicemia followed excision of an infected, acquired

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"The first medical cure of subacute *Streptococcus viridans* septicemia superimposed upon congenital arteriovenous communication (patent ductus arteriosus) reported by Touroff, Leach in 1936."

arteriovenous aneurysm of the right external iliac artery and vein. These authors emphasized that surgical excision of an infected arteriovenous aneurysm is futile in cases in which vegetations coexist in the heart. For under such circumstances, even though the aneurysm is removed completely, the cardiac vegetations will continue to act as a focus for perpetuation of the sepsis. Thus, operation is contraindicated in cases of mycotic arteriovenous aneurysm occurring as a complication of subacute bacterial endocarditis. For the same reason, operative treatment also is contraindicated in cases of infected, primary arteriovenous aneurysm in which the cardiac valves have become involved secondarily. Accordingly, the only cases which remain amenable to surgical treatment are those of infected, primary arteriovenous aneurysm in which infection has remained confined exclusively to the local site. Under the latter circumstances, local excision of the aneurysm may result in cure.

Since the report of Hamman and Rienhoff, no other instance of cure of subacute *Streptococcus viridans* septicemia following excision of an infected arteriovenous aneurysm has been recorded in the literature. It therefore appears warranted to report a second successful case in detail.

REPORT OF CASE

R W, a native born white male aged 26 years, single and a clerk, was admitted to the consultation service of The Mount Sinai Hospital on February 2, 1941, because of fever, malaise, and progressive weakness of approximately 1½ years' duration. During childhood he had had measles, pertussis, and scarlet fever, without sequelae. The surgical history included a bilateral inguinal hernioplasty performed at the age of 5, and a tonsillectomy performed at the age of 7 years.

On entering high school at the age of 14, he was examined by a physician and, because of "frail constitution," was advised to abstain from strenuous athletics. No evidence of any cardiac abnormality was present at the time. Despite the advice of his physician, he participated actively in athletics, including bicycle riding, running, and swimming, without manifesting unusual distress or shortness of breath.

At the age of 17 years—9 years before the present admission—the patient suffered an accidental thigh and through gunshot wound of the left thigh. Although bleeding was profuse, he responded well to

treatment and was discharged from a local hospital, symptom free and with the wounds practically healed, at the end of 1 week. Shortly thereafter, he became aware of a peculiar "buzzing sensation" in the thigh. Because this was not associated with other obvious abnormalities, he considered it to be of no importance and failed to mention it when the history was first taken. About a year after the accident he began to suffer from fatigue and dyspnea on exertion. A diagnosis of "chronic heart disease" was made by the patient's physician at the time, but the nature of the cardiac abnormality and its relationship to the previous injury of the thigh apparently was not recognized. He was told however, that his blood pressure was 148/58, and his pulse rate 122. During the next 6 years he continued his activity as a student and then as a clerk, the symptoms of weakness, dyspnea on exertion, and cardiac palpitation becoming increasingly severe.

About 2 years prior to admission to the consultation service, a decayed molar tooth was extracted and the root canal of an adjoining devitalized tooth was filled. Soon thereafter he became acutely ill, with fever and malaise. Loss of weight, strength, and appetite, followed shortly. All of these symptoms, in addition to the pre-existing dyspnea and palpitation, continued with remissions and exacerbations during the next 8 months. About 1½ years prior to admission he suffered an attack of severe left-sided pleuritic pain associated with productive cough, but without hemoptysis. Evening rises of temperature to 103 degrees F and drenching sweats then began. These symptoms at first caused only periodic confinement to bed, but during the 3 months prior to admission the fever, sweats, and weakness, became so severe that he was bedridden most of the time. During the last month he suffered another attack of left-sided pleuritic pain and three shaking chills each lasting about 20 minutes.

During the year preceding admission he had received large doses of sulfanilamide, and during the last 3 months he had been kept continuously on sulphyridine therapy.

Examination. The patient first came under the observation of one of us (H L) in the consultation service, February 15, 1941. At that time examination disclosed a thin, pale, sweating, somewhat dyspneic young man who appeared acutely and chronically ill. The temperature was 102 degrees F, pulse rate 126, and respiratory rate 22.

A summary of the essential findings follows. Arterial pulsations were distinctly visible in the vessels of the optic fundi. Forceful pulsations were present in the suprasternal and subclavicular areas, and harsh murmurs were noted over the carotid and subclavian arteries. Cardiac action was regular, the apical rate being 126 per minute. The heart was moderately enlarged to the left on percussion, diffuse forceful pulsations being noted in the fourth and fifth intercostal spaces outside the midclavicular line. The first sound here was loud and booming. The second pulmonic sound was louder than the



Fig. Preoperative roentgenogram of chest. Note enlargement of heart to the left and pulmonary vascular congestion.

secondortic sound. Over the apex and pulmonary area, short, soft, high pitched, blowing systolic murmurs were present. All pulses were of the collapsing (Corrigan) type. The arteries of both lower extremities pulsated freely, the pulsations of the vessels on the left being more forceful than those on the right.

Small, almost invisible, scars were present over the lateral and medial aspects of the midportion of the left thigh. At the same level, a plum sized epimastoma mass, embedded within the muscles close to the inner aspect was palpable. Over this mass, coarse thrill and harsh to-and-fro machinery murmur were readily audible. The left common femoral artery was obviously enlarged on palpation and could be seen to pulsate very vigorously. The to-and-fro murmur in the thigh could be heard down to the knee and over the great vessels of both legs. The left thigh, leg, and foot were warmer than the right. The diameter of the left thigh was greater than that of the right. The superficial veins of the left leg and foot were prominent.

The liver was palpable for a distance of three fingerbreadths, and the spleen for a distance of four fingerbreadths, below the costal margin. No petechiae, Osler nodes, or Janeway lesions were noted. The fingers were clubbed, lightly and capillary pulsation of the nail beds was increased.

The blood pressure in the right arm was 3/70, in the left arm 24/60. In the right thigh 60/70, and in the left thigh 180/0. On firm compression of the pulsating mass in the left thigh, the pulse rate decreased from 110 and the blood pressure in the right and left arms rose to 35/80, and 3/74 respectively. Oscillometric readings at the right

thigh, calf and ankle were 33/16, and 3/6 respectively. At the same levels on the left they were 20, 43/6 and 3/6.

Laboratory data. A teleroentgenogram revealed enlargement of the heart to the left and the presence of pulmonary vascular congestion (Fig. 1). On fluoroscopy the left ventricle appeared dilated. The left auricle was not enlarged, and the general configuration of the heart was not that usually noted with valvular disease. The electrocardiogram revealed sinus tachycardia, the rate being 105 p.m.m. to. Right axis deviation was present. *RT* and *RT* were depressed slightly and *T* inverted the tracing suggesting either right ventricular hypertrophy or vertically placed heart. Upon compression of the left femoral artery the rat slowed from 5 to 90 per minute, *RT* became isoelectric and *T* upright. Upon release of compression the rat returned to 5 and *RT* and *T* assumed their original abnormality. The phonocardiogram revealed systolic murmur and a short, early diastolic murmur in the pulmonary area. The cardiac output was 7.2 liters per minute and fell to 5.5 liters upon compression of the left common femoral artery.

X-ray examination of the abdomen revealed marked enlargement of the liver and spleen. X-ray examination of the lower extremities revealed a small irregular area of calcification in the midportion of the left thigh, medial to the shaft of the femur. The specific gravity of the urine ranged 1.010 to 1.020. Albumin and dextrose were absent. The microscopic examinations were essentially normal. The blood contained 4,850,000 red cells per cubic millimeter. The hemoglobin content was 6 per cent. There were 9,000 white cells, of which 70 per cent were segmented polymorphonuclear leukocytes, 1 per cent unsegmented polymorphonuclear leukocytes, 6 per cent lymphocytes, and 2 per cent monocytes. The color index was 7. The smear revealed chromia polychromasia, and anisocytosis. The erythrocyte sedimentation rate was 20 mm/hr. (markedly accelerated). The Wassermann and Kahn tests gave negative results. The blood agglutination reactions for *Bacillus abortus* and *Bacillus melitensis* were negative. Blood cultures on two occasions yielded *Streptococcus viridans* (alpha) 5 colonies and 1 colony per cubic centimeter respectively.

For the sake of clarity the history and laboratory data have been presented in sequential order. Actually the complete history was elicited with difficulty and it was not until all the details finally were learned that appropriate clinical and laboratory investigations were carried out. For example when first questioned the patient omitted entirely the history of gunshot wound of the thigh. In view of the negative past history of rheumatic fever and cardiac symptoms during



Fig. 3 Interior of excised specimen. Probe passed through proximal artery enters aneurysm from above. Proximal vein is completely obliterated by scar tissue. Lower probe enters aneurysmal sac through the distal artery. Not that the distal ein is widely dilated and, extending downwards from the point of bony constriction forms the lower half of the aneurysm. Diverticula (false aneurysms) are present in upper half of sac. Not particularly the scattered vegetations within the interior of the upper half of the sac and the large triangular excision within the lower half of the sac. Specimens taken from these vegetations revealed large numbers of streptococci, which on culture were reported as *Streptococcus viridans*.

femoral artery and vein were markedly dilated. Below the aneurysm, the deep femoral vein was found to be the site of enormous fusiform dilatation; the deep femoral artery was of very small caliber. Numerous collateral vessels, both arteries and veins, entered the main sac. The accessory sac was quite free of collaterals and apparently represented a false aneurysm—the result of a hematoma formed at the time of the original injury.

The profunda femoris artery and vein, both the aneurysm, were doubly ligated with heavy silk thread, and divided. All collateral vessels, entering and leaving the sac, also were ligated and divided. Finally the two main vessels below were ligated and divided, and the entire lesion was removed en masse.

Owing from the dead space within the adductor muscles controlled by temporary packing, and the wound closed by loose appositioning the deep fascia of the thigh. The skin closed with clips. No drainage was employed. A transfusion of 500 cubic centimeters of citrated blood was administered at the conclusion of the operation.

Description of specimen. The specimen consists of a shrunken retroperitoneous aneurysm received in situ, which in the opened state measures 7.5 by

6 cm in its largest diameters. The artery proximal to the aneurysm measures 4 cm in length. It appears thin and elastic. The proximal ein is 5 cm long and is entirely obliterated by dense fibrous tissue. The proximal vessels open into a multilocular cavity lined by endothelium. The distal artery measures 3 cm in length and is patent. The distal vein, which is approximately 3 cm long, is the site of fusiform dilatation measuring 4 cm across when opened. At the ostium of the distal vein there is a constriction below which the enlargement of the distal vein takes place. Between the ostia of the arterial and venous channels, but below the ridge is present. Thus, the opened specimen assumes an hour glass appearance. Connected with the true aneurysmal sac there are diverticula (false aneurysms) each 1 cm in length. A third diverticulum the size of a large hazel nut appears to be obliterated by thrombus; the surface of which is covered by endothelium. Red and gray irregular vegetations, varying in size from the head of a pin to peas, stud the saccular portion of the aneurysm. The more fusiform portion, formed by the dilated proximal portion of the distal vein, is the site of large, flat, triangular organizing grayish red vegetation. The interior of the fusiform portion of the aneurysm presents many sclerotic plaques. The outside of this portion of the aneurysm also presents a calcific plaque. Flat, sclerotic plaques also are present within the wall of the specimen (Fig. 3). (It is of interest to note that these calcific masses are discernible on preoperative roentgen examination of the left thigh.)

After the report. Arteriovenous aneurysm showing subacute bacterial endovascularitis (numerous gram-positive cocci; found within the vegetations).

Bacteriological report. Culture of vegetations which were obtained from within the arteriovenous aneurysm yields heavy growth of the *Streptococcus viridans*.

Postoperative course. The patient immediately after operation was extremely satisfactory. By the third postoperative day sinking laparotomy incision the general appearance and condition as noted. At that time the cardiac murmurs were almost inaudible, the pulse rate considerably slower and had lost its collapsing character. The highest postoperative temperature was 38.6 degrees F on the second day. Thereafter it receded progressively and as normal by the 8th postoperative day. The wound as healed by primary union in 6 days and 4 days later the patient permitted out of bed. By the 10th postoperative day the systolic murmur at the apex had disappeared. A short, harsh diastolic murmur was heard over the pulmonary area, only on complete inspiration. The bruit and thrill over the thigh had disappeared. The liver no longer as palpable. The spleen greatly reduced in size but still could be palpated one finger breadth below the costal margin. Four days later the spleen no longer as palpable.

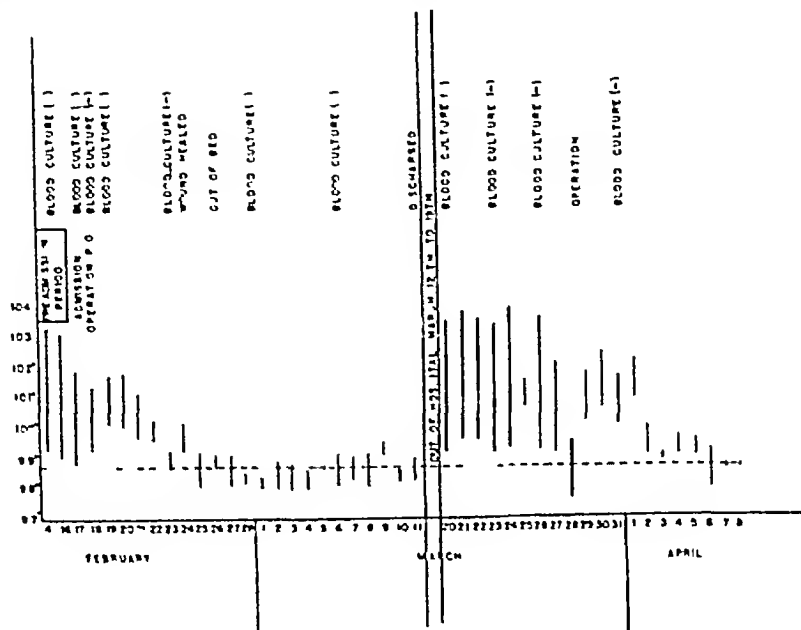


Fig. 4. Graphic chart indicating temperature and blood cultures in relationship to operations.

The first blood culture, taken 4 hours after operation, was reported sterile after 14 days of incubation. Four additional blood cultures were taken on the 1st, 5th, 10th, and 16th postoperative days respectively (Fig. 4). These likewise were reported sterile after 14 days of incubation. No chemotherapy was administered during the postoperative course and accordingly the prompt disappearance of organisms from the blood stream could be ascribed only to the operative procedure. The patient was kept in the hospital for 21 days following operation in order to observe him closely and to repeat various investigative studies (Tables I, II, III). At the time of discharge, the temperature had been essentially normal for 2 weeks, and he was gaining weight and appeared to be in excellent general physical condition.

Subsequent course. Three days after returning home, the patient experienced a sensation of fullness and pressure in the abdomen. The following day severe diarrhea developed and the temperature rose to 100.4 degrees F. During the next 5 days irregular fever, ranging as high as 103.6 degrees F, and nightly sweats were present. Accordingly, he was advised to re-enter the hospital for investigation.

On admission March 20, 1941, to the medical service of Dr. George Bachr, temperature was 101.4 degrees F, pulse 92, and respirations 20. He did not appear acutely ill and his general condition seemed even better than when last observed. The cardiac findings were unchanged except for the presence of a short faint high pitched apical systolic murmur which presumably was of functional origin. The blood pressure in the extremities was essentially the

same as at the time of discharge 9 days previously. The liver was not palpable. The spleen however again was palpable 2 fingerbreadths below the costal margin. The operative wound was well healed and all clinical evidence of the previously existing arteriovenous aneurysm was absent.

A x-ray examination of the chest disclosed further diminution in the size of the heart and previously prominent pulmonary vessels. The electrocardiogram revealed no change as compared with the tracing made shortly before discharge from the hospital. The phonocardiogram revealed a faint systolic murmur over the precordium, a tracing made over the region of the femoral vessels on the left side failed to reveal the presence of abnormal sounds. The specific gravity of the urine was 1026.

Albumin and dextrose were absent. The microscopic examination was negative. The hemoglobin content of the blood was 70 per cent. There were 4,600 leucocytes per cubic millimeter of which 44 per cent were segmented polymorphonuclear leucocytes, 20 per cent nonsegmented polymorphonuclear leucocytes, 19 per cent lymphocytes, 5 per cent monocytes, and 3 per cent eosinophiles. A blood smear did not reveal macrophages. The erythrocyte sedimentation rate was normal. Culture of the stool revealed only enterococci and *Bacillus coli*.

Three blood cultures, performed during an 8 day period of observation, were negative after 14 days of incubation. Blood agglutination tests for heterophile anti body, dysentery, typhoid, paratyphoid, *Bacillus abortus*, and *Bacillus melitensis* also were negative. During this period, the temperature ranged between

TABLE I.—STUDIES OF THE CIRCULATION

	Before operation	After operation
Character of pulse	Cerebral	Ketoid
Left common femoral artery		
Size	Large	Smaller
Pulsation	Marked	Normal
Right arm (brazed)	B.P. 11/70	B.P. 11/60
Comparison of left common femoral artery	90	75
Left arm (brazed)	12/70	100
Comparison of left common femoral artery	100	100
Right thigh	240/70	20
Left thigh	180/70	100
O-oscillations	Right 240	Left 100
Thigh C.M.	1	7
Table	1	3

90 and 93.8 degrees F and the pulse rate between 8 and 20. In spite of the irregular fever the patient continued to look quite ill, and various circulatory studies confirmed the absence of the peroneal existing arteriovenous communication.

In view of the pre-existing infection, it appeared essential to exclude recurrence of sepsis as the cause of the symptoms. It was postulated that if sepsis were present, it most likely was derived either from previous unrecognized endocarditis or from a thrombophlebitis involving vascular channels immediately adjacent to the former site of the arteriovenous aneurysm. However the diagnosis of recurrent subacute *Streptococcus viridans* septicemia appeared to be excluded by the negative blood cultures. (In an effort to exclude the diagnosis of thrombophlebitis in closing vascular channels in the thigh, one of the blood cultures was taken directly from the left common femoral vein.) Furthermore, the erythrocyte sedimentation rate now was normal and leukopenia as present. Finally the re-enlargement of the spleen seemed too marked and too rapid to be consistent with the diagnosis of subacute bacterial septicemia. The history of abdominal pain and diarrhea at onset, together with the acute en-

TABLE II.—STUDIES OF THE CIRCULATION

	Before operation	After operation
Venous pressure	1 cm H ₂ O	0 cm H ₂ O
Right upper quadrant pressure		
Systolic	100	100
Diastolic	60	60
Cardiac output		
Mean	1 L/min	1 L/min
Comparison of common femoral artery anastomosis after release	1 L/min	1 L/min
Cardiac anastomosis (anastomosis)		
Anastomosis	Soft, pulsatile	None
Pulsation	Normal	None
Heart		
Size of myocardium	Large	Normal
Pulsation (normal artery)	Present	Present

largement of the spleen and leukopenia, suggested the possibility of an intercurrent typhoid or paratyphoid infection. However these diagnoses are excluded by appropriate examinations of the stool and blood. Finally in view of the fact that the patient had received a number of transfusions during the first admission, the diagnosis of accidental splenic infarction as entertained. The rapid splenic enlargement and leukopenia appeared to be consistent with such diagnosis but several blood smears proved negative for plasmodia. After consultation with Dr Harold Verboet it was decided as a precautionary measure to re-explore the original operative site for evidence of local thrombophlebitis. In view of the fact that the blood cultures were sterile it was considered possible that such a focus might be found. Furthermore, it was the consensus that even if exploration proved negative no harm could result.

On March 28, 1941 an operation was performed (b. A. S. W. T.) under ethyl ether anesthesia. The incision was begun at point above Poupart ligament and carried down to medial to the old operative scar at the junction of the upper and middle third of the thigh. The common femoral artery and vein were exposed and found to be of approximately normal caliber. (The artery measured approximately 3/8 inch and the vein 1/8 inch in diameter.) The common femoral and superficial femoral arteries were freed and retracted laterally in order to expose the point of confluence of the superficial femoral vein and the short, proximal stump of the previously excised deep femoral vein. A bore hole was made in or about these structures. The common femoral artery was divided between ligatures at the level of Poupart ligament. The vein then was freed in downward direction and the stump of the deep femoral vein, together with a 4 inch section of the superficial femoral vein was removed. Coming from the surrounding tissue

TABLE III.—ELECTROCARDIOGRAPHIC STUDIES

Comparison of Left Common Femoral Artery	Before operation	After operation
Pulse rate	100/min	90/min
Before compression	100/min	90/min
After compression	100/min	90/min
ECG	Right	Right
T wave, lead III	Inverted	Inverted
Before compression	Inverted	Inverted
After compression	Inverted	Inverted
RT, lead III	Inverted	Inverted
Before compression	Inverted	Inverted
After compression	Inverted	Inverted

controlled by a small gauze packing which was left *in situ* and brought out through the lower angle of the wound. The fascia was sutured loosely and the skin was closed with clips.

The pathological report upon the excised specimen was as follows: "Vein showing focal phlebosclerosis, otherwise no significant change is present."

The immediate postoperative reaction was satisfactory. During the first 3½ days, the temperature ranged between 100 and 102.4 degrees F. A blood culture, taken on the third postoperative day, was reported sterile. Four grams of sulfapyridine was administered on the day of operation and 6 grams on the first postoperative day. The temperature became normal on the 5th day after operation.

The wound healed kindly, the drain and the skin clips being removed on the 5th postoperative day. By the 7th postoperative day, the spleen had diminished appreciably in size. The patient was discharged on the 11th postoperative day in good physical condition. At the time of discharge there was moderate edema of the left lower extremity.

When last observed in the follow-up clinic on March 17, 1942, the patient had gained 42 pounds in weight and was entirely free of symptoms. The operative incisions were well healed, and edema of the left lower extremity, noted after the second operation, no longer was present. The spleen was not palpable. The heart was essentially normal in size. The blood pressure was 122/74. The electrocardiogram was normal. The cardiac output was normal (4.6 liters). The phonocardiogram revealed a very faint systolic murmur over the precordium which was interpreted as being of functional origin. A sound tracing taken from the thigh failed to disclose any abnormality. On the basis of the complete absence of symptoms and with the findings herein noted, recovery from both the arteriovenous aneurysm and subacute *Streptococcus viridans* bacteremia was considered to have taken place.

SUMMARY

The patient, a male aged 26, suffered a through-and-through gunshot wound of the left thigh 9 years previously. Within a year of the injury, evidence of an arteriovenous aneurysm associated with manifestations of cardiac insufficiency developed. Although the diagnosis of a "heart condition" was made, the existence of an arteriovenous aneurysm was not recognized. Following the extraction of a tooth and some dental reparative work, 7 years after the original injury, symptoms of sepsis began. The manifestations continued for almost 2 years before the diagnosis of arteriovenous aneurysm and subacute *Streptococcus viridans* septicemia was made. Clinical and laboratory investigations failed



Fig 5 Roentgenogram of chest 6 months after excision of arteriovenous aneurysm. Note reduction in size of heart.

to reveal conclusive evidence of an infective endocardial lesion as the source of the sepsis. It therefore was postulated that the focus of infection was situated within the arteriovenous aneurysm. Under the circumstances, surgical excision of the aneurysm appeared to offer a hope of cure. At operation, a large arteriovenous aneurysm involving the profunda femoris artery and vein, and filled with vegetations containing *Streptococcus viridans*, was found and excised widely. The course following operation was one of rapid improvement, the local and constitutional manifestations of arteriovenous aneurysm disappearing rapidly and the blood cultures becoming sterile promptly. In view of the fact that chemotherapy had been administered prior to operation for one year without effect and was not administered at all after operation, the sharp termination of the sepsis appeared attributable solely to the operative removal of the infected aneurysm. The patient was discharged from the hospital 3 weeks after operation in excellent physical condition, all postoperative blood cultures having been reported sterile.

He was readmitted 9 days later because of abdominal pain, diarrhoea, recrudescence of septic temperature, and enlargement of the

spleen. During an 8 day period of observation 3 blood cultures including one taken directly from the left common femoral vein were reported to be sterile. After a number of infectious diseases including typhoid fever and malaria has been excluded it was decided to re-explore the old operative site for evidence of thrombophlebitis despite the negative blood cultures.

At operation no abnormality was found locally but the common femoral vein the upper portion of the superficial femoral vein and the stump of the deep femoral vein were excised as a precautionary measure. Microscopic examination of the specimen failed to reveal the presence of any significant changes. Following operation recovery ensued rapidly.

One year has elapsed since the last operation and the patient remains entirely well. This is the second case of acquired arterio-

venous aneurysm complicated by subacute Streptococcus viridans septicemia in which recovery has followed surgical treatment.

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CONTRAST MEDIA IN CYSTS AND ABSCESES OF THE CEREBRAL HEMISPHERE

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THE effectiveness and ease of performance of any technical procedure is enhanced by its simplification. Thus in surgery, that approach to a large, deep seated lesion which is most direct is the one of choice, provided vital structures are not traversed.

It has been the experience of all neurosurgeons in attempting ventricular air injection or biopsy of a cerebral tumor, to enter unexpectedly a cystic cavity with the exploring needle, xanthochromic fluid or pus being obtained. To approach such a lesion in the most direct manner and thus simplify operative procedure, the use of a contrast medium is desirable.

Air and iodized poppy seed oil have been used for this purpose but do not mix with fluid contents. Sodium iodide is miscible and Rocky instilled a 20 per cent aqueous solution into a brain abscess to show "the post-operative course after the original drainage had been instituted." The visualization in this case was excellent. It showed, moreover, how a portion of the collapsed abscess capsule had wrapped itself around the drainage tube and caused loculation of the abscess cavity rather than the desired evacuation. Colloidal thorium dioxide (thorotrast) is less irritating than sodium iodide, mixes readily, and has the added advantage of being phagocytized by the cellular elements of an abscess wall, making the capsule radio-opaque. This has been previously demonstrated by me. Jensen first reported the use of colloidal thorium dioxide for ventriculography. In a discussion on this same subject, Freeman and Schoenfield suggested that this contrast medium be used in cysts or encapsulated abscesses of the brain.

The following histories are selected from a small group of cases in an effort to show the value of colloidal thorium dioxide cystography.

From the Department of Surgery, The University of Michigan Clinic of Dr. Max M. Peet

CASE 1. A L., a 14 year old girl, entered the University Hospital with a 6 months' history of gradually increasing intracranial pressure. There was found on examination marked papilledema and a quadrantic type of homonymous hemianopsia but little else in the way of localization.

A ventriculogram was performed which gave evidence of a large expanding lesion of the left cerebral hemisphere. A trephine opening was then made on the left, a half inch above and behind the ear. A cyst was entered with the exploring needle close to the surface of the brain. Twenty cubic centimeters of somewhat viscous xanthochromic fluid was removed and 5 cubic centimeters of colloidal thorium dioxide (thorotrast) was injected.

Röntgen ray studies revealed a large cyst. A lateral film, taken with the forehead up allowing gravity to aid in filling out the posterior wall of the cavity, revealed a perfectly smooth contour. A lateral film with the forehead down, however, outlined a mural nodule attached to the anterior wall (Fig. 1).

Under avertin anesthesia, the trephine incision of the left side was carried forward and superiorly in the shape of a hockey stick. The temporal muscle was stripped downward, thus exposing the squama of the temporal bone. Trephine openings were made to center a small bone flap directly over the mural nodule. These were connected with the Gigli saw, and the bone was removed to be replaced as a free graft. The dura was opened. The underlying brain substance was extremely thin and an opening was made into the cyst. The mural nodule which was about the size of an English walnut was seen anteriorly exactly as pictured in the x-ray film. It was widely excised with the electrosurgical unit.

Convalescence was uneventful and the patient was discharged on the tenth postoperative day. She has remained well for the past 2 years. There has been no change in the hemianopic defect except for some concentric contraction which was attributed to secondary optic atrophy. The tumor was shown microscopically to be a fibrillary astrocytoma.

This lesion, as the ventriculogram suggested, was of considerable size. Judging from the air studies alone, to have exposed it completely would have meant turning down a large bone flap. Cushing long ago showed that if the mural nodule of an astrocytoma were removed the cyst wall need not be dealt with. By accurately visualizing the mural



Fig 2 Case 2 Ragged irregular outline of the cyst of a glioblastoma multiforme

Consequently, the cyst is always surrounded by solid or semisolid necrotic tumor and the wall is poorly defined. On surgical incision into such a cavity it tends to obliterate due to the rapid expansion on all sides of the broken down, edematous, discolored tumor tissue. One might draw a comparison between this lesion and the unencapsulated abscess of the brain secondary to pulmonary suppuration (Fig 3). Both form their cavities by a process of liquefaction necrosis without any tendency toward walling off. There is consequently a certain resemblance as shown by contrast media.

From the above discussion I have reached the following conclusion. If on attempting biopsy or ventriculogram, a cyst is entered it should be outlined by the injection of colloidal thorium dioxide. If a ragged, irregular cavity is demonstrated one may be fairly certain of the diagnosis of glioblastoma multiforme or at least, of a malignant glioma. The tumor must, of course, be subjected to biopsy examination for confirmation and in this procedure, again, the contrast medium is of value in showing where best to take the specimen. Microscopic diagnosis from biopsy material

is admittedly not infallible, but the presence of a malignant type of growth can usually be determined. Every case is a law unto itself but if the rolandic area or the various speech centers are involved, operation is inadvisable.

CASE 3 H O, a 57 year old male, was admitted to the Hospital in a stuporous condition. He could be roused enough to demonstrate a left sided hemiplegia which seemed complete. There was a previous 6 months' history which was undoubtedly related to a cerebral lesion.

On attempting ventricular oxygen injection through a trephine opening, a half inch above and behind the right ear as is the usual procedure in this clinic, a cyst was entered and dark xanthochromic fluid was obtained. Between 6 and 8 cubic centimeters of colloidal thorium dioxide were introduced. X-ray studies gave evidence of a temporoparietal cyst with a large mural nodule (Fig 4).

The patient was returned to the operating room and under local anesthesia, a moderate sized bone flap was turned down directly over the lesion. The cyst was entered after traversing a little less than a centimeter of brain substance. At the posterior medial aspect of the cyst wall an irregular brownish mural nodule about the size of a large plum was found. This was completely excised together with the cyst wall until normal white substance was everywhere encountered, the tumor having been thought to be a cystic oligodendroglioma. (Cushing and Eisenhardt have shown that this type of tumor



Fig. Case 3. left, Lateral roentgenogram with forehead up showing smooth posterior wall outlined by 5 cubic centimeters of colloidal thorium dioxide which has thor-

oughly mixed with the fluid contents of the cyst. Right, Lateral projection with forehead down outlining the neural arches anteriorly.

nodule in this case an effective operation was carried out by means of a comparatively simple procedure. It is doubtful if 50 cubic centimeters of air could have demonstrated this lesion as well as 5 cubic centimeters of colloidal thorium dioxide.

CASE 3 J. G., a 6 year old man, was admitted to the hospital because of difficulty in speaking and headache both of which had been present for 3 months.

On examination the usual fields revealed suggestive right homonymous hemianopsia but no papilledema. There was slight right sided hemiparesis. The patient had mixed expressive receptive type of aphasia. No definite right sided sensory changes could be elicited but the patient was unable to co-operate fully. A diagnosis was made of lesion of the left temporoparietal region, probably tumor.

A trephine opening was made on the left, an inch above and half an inch behind the top of the ear (this is somewhat higher than the usual opening made in this clinic for ventricular air injection). When the dura was opened, the cortex appeared normal. At a depth of about 3 centimeters, cyst entered with the exploring needle though there

was no unusual sense of resistance. About 5 cubic centimeters of viscous yellow fluid was obtained and 5 cubic centimeters of colloidal thorium dioxide

instilled. X-ray studies were completed after closure of the wound and demonstrated a deep seated cavity with an irregular ragged wall (Fig. 3).

The patient was returned to the operating room here biopsy specimen was taken with the hollow needle. The microscopic diagnosis glioblastoma multiforme. The patient was discharged as hopeless on the fifth postoperative day.

The glioblastoma multiforme because of its microscopic infiltrative growth defies surgical removal. Though biological or physicochemical methods of treatment may be developed in the future the fact remains that this lesion does not respond to gross surgical excision, roentgen ray therapy or both. The first real contribution to the palliation of this lesion was the "internal decompression" of McKenzie. Spurling, on the other hand, when a glioblastoma multiforme is strongly suspected takes a biopsy specimen and does not ordinarily operate if the microscopic examination brings confirmation.

Cyst formation is common in the glioblastoma multiforme and is undoubtedly due to central necrosis within the tumor wall.



Fig 4 Case 3 Cystogram of tumor diagnosed as primary sarcoma of brain

ness of the left leg Babinski's sign was negative bilaterally. There was a leucocytosis of 20,000. A pansinusitis on clinical examination was confirmed by x-ray studies.

A diagnosis of subdural abscess was made. Inasmuch as the infection was thought to have extended through the right frontal sinus, epidural pus was also suspected. It was decided first to perform a right sided Killian operation.

At operation by Dr. James Maxwell of the department of otology, an empyema of the right frontal sinus was found. The entire wall of the frontal sinus was removed but there was no evidence of erosion of the inner table. The ethmoidal cells were found to be grossly infected and were extirpated. The anterior face of the sphenoid was removed and the sphenoid found to contain thick pus. The inner table of the frontal sinus was removed but there was, in this case, no evidence of epidural pus or even granulation tissue over the tense dura. It was thought best to expose the dura through a clean field above the operative site. It was believed that the patient's condition warranted waiting until the following day before this procedure was carried out.

The patient was carefully watched for the next 24 hours since any further evidence of acute increase in intracranial pressure would have necessitated immediate operation.

At the end of this period the patient's condition was unchanged. Under local anesthesia, a trephine opening was made over approximately the center of the frontal bone. The dura appeared tense and bluish than normal. When the dura was opened there was an escape of a large amount of thick green

ish white, odorless pus which was extra-arachnoid. The incision was now enlarged and an area of bone about the size of a silver dollar was removed with the rongeur. The dura was further opened in a stellate manner, the pus extending in all directions. There now developed a herniation of the brain through the defect, making retraction of the brain impossible. In order to gain relaxation so that all pus could be removed and adequate drainage be established without making a tremendous bone defect, it was decided to perform a lumbar puncture.

The patient was turned and the lumbar puncture needle was introduced. The pressure was between 600 and 700 millimeters of water. The fluid was cloudy and contained 5,600 cells per cubic millimeter. After approximately 50 cubic centimeters had been obtained, the brain commenced to pulsate and to drop away from the dura. With the lumbar puncture needle left in place, the surface of the brain was now easily depressed with a lighted retractor, the entire surface of the brain being explored back to at least the midparietal region. All pus was removed by suction even as far forward as the tip of the frontal pole. The wound was washed out with Ringer's solution and hydrogen peroxide, inasmuch as it was thought that the pus could not be extended any farther than it had already gone. Rubber tissue drains were inserted as far as possible in four directions, to the postparietal region, the midline, the tip of the frontal pole, and down onto the temporal lobe near its tip. This procedure was carried out without difficulty and with almost no trauma to the arachnoid since the hemisphere following lumbar puncture retracted from the dura for

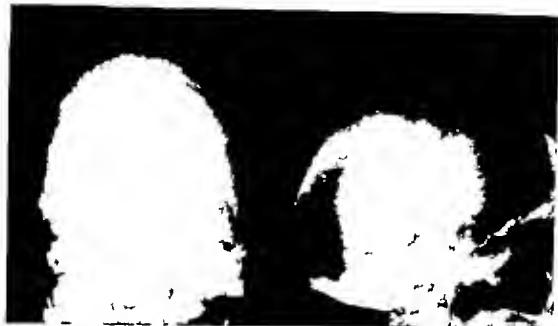


Fig. 3. Outline typical of unencapsulated abscess metastatic from pulmonary suppuration.

tends to recur rapidly.) During this process it was found that tumor substance extended posteriorly almost to the occipital pole, basally to the inferior surface of the temporal lobe and anteriorly to the midparietal area. The compressed right lateral ventricle was entered and the choroid plexus clipped. The upper surface of the tentorium was widely exposed and to some extent the right side of the falx.

The patient made excellent convalescence except for complete left homonymous hemianopsia (with splitting of the macula). The tumor, as histologically thought to be primary sarcoma of the brain.

The patient returned 8 months later in semicomatose condition. Operation was again performed and enormous recurrence was found. Again the tumor seemed to be completely excised. Immediate convalescence from the second procedure was surprisingly good but he returned 3 months later and died. The autopsy which was limited to the head, revealed massive recurrence.

This tumor from the point of view of cystography with colloidal thorium dioxide might be considered as midway between a benign lesion and a malignant one. The fact that the cyst was extremely large suggested the former while the size of the mural nodule and the slight irregularity of the cyst wall was in favor of the latter. Where there is real doubt as to operability direct attack

upon the lesion itself rather than biopsy is indicated.

The following case is reported in detail, first as a method of handling an acute subdural abscess and second because a contrast medium was of such help in dealing with a complicating cerebral abscess.

CASE 4. A 7-year-old boy entered the University Hospital with the following history. Two weeks previous to admission the patient had suffered an ordinary head cold. This began to subside within few days but bilateral frontal headache persisted. One week before admission the headache became more severe on the right and swelling of the right upper eyelid developed rapidly. Two days later, the swelling had reached peak and rapidly subsided. There as now noted, besides increasing headache stiffness of the neck and increasing irritability. Two days before admission, nausea and projectile vomiting developed and numbness of the left hand was complained of. This was rapidly followed by weakness of the entire left side.

Examination revealed an extremely ill and apathetic patient. The temperature was 38 degrees, the pulse 78 and respiration 20. There was stiffness of the neck and positive Kernig sign. Fundoscopic examination revealed early papilledema. There was a left central type of facial paralysis and the tongue deviated to the left on protrusion. There was marked weakness of the left arm and slight weakness

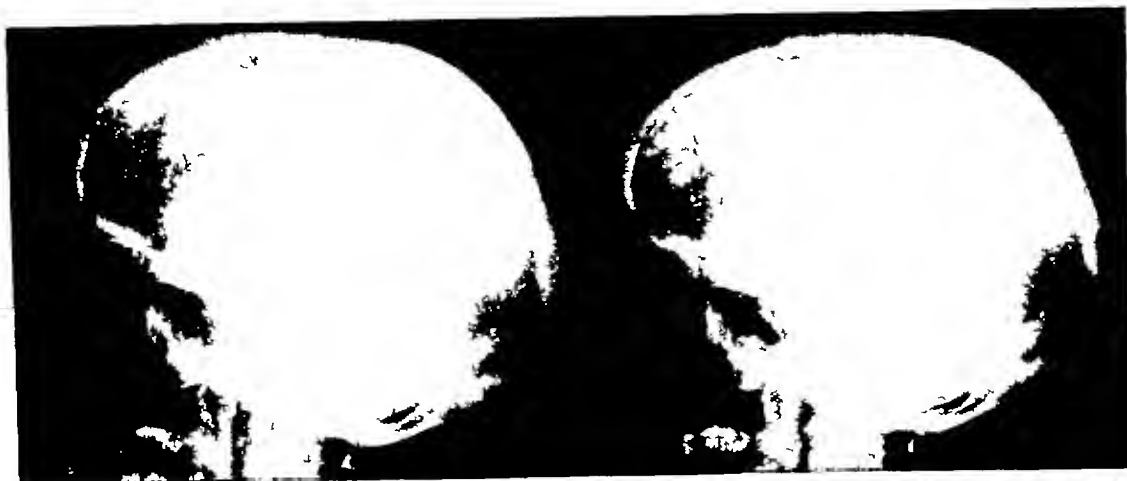


Fig 6 a, left, Decompression was placed too high because the abscess was not visualized previously b Three

days later the capsule is shown to have risen toward the decompression

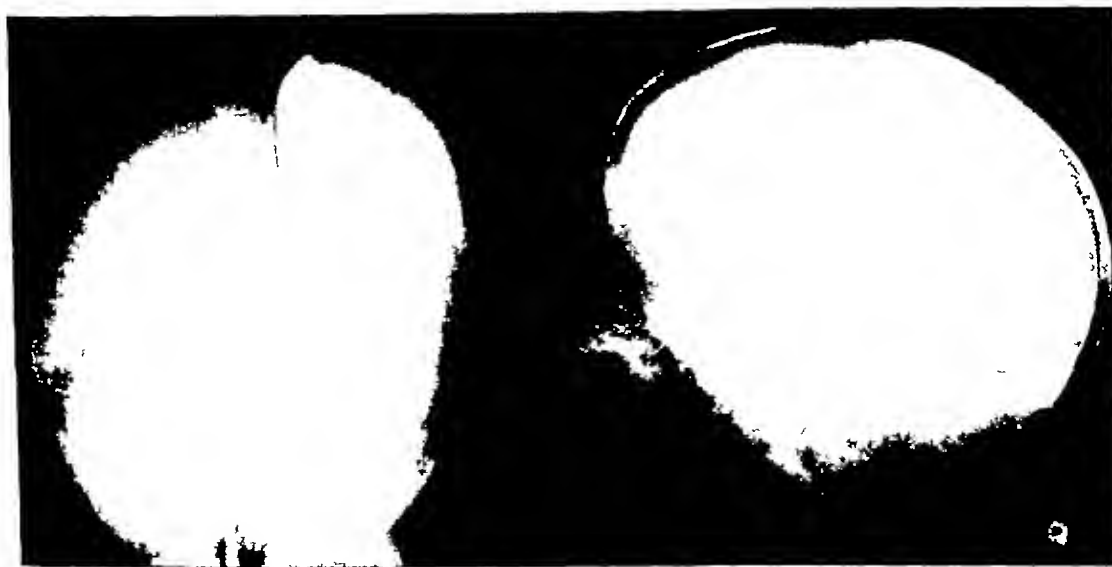


Fig 7 Case 5 Colloidal thorium dioxide thoroughly mixed with pus in infected subdural hematoma

formed at that time without difficulty. The most recent x-ray films which were taken 3 months after operation show stereoscopically a fine circular line less than 1 centimeter in diameter in the substance of the brain just above the tegmen tympanum. This is undoubtedly due to colloidal thorium dioxide in what remains of the capsule. It is probably of no significance as the patient is back at full time work, but it will be followed with interest.

CASE 5 R. F., a 7 months old male infant, was admitted to the hospital with the appearance of being *in extremis*. The child according to the parents' story, had been well up to the age of 4 months at which time he had developed bilateral otitis media and a pneumonia which was confirmed by x-ray. This had gradually cleared but a spastic tetraplegia with enlargement of the head had developed.

On examination the infant was found to weigh but 10 pounds. Though the head was generally enlarged this was most marked on the left side. There was no papilledema. The leucocyte count was



Fig. 5. Case 4. a, left, Encapsulated abscess of brain secondary to subdural abscess. The large anterior skull defect as made for drainage of the subdural abscess, the trephine opening just posterior as used for the injection

at least 1.5 centimeters in all directions. The drains were gradually removed within the course of the next 4 days. Convalescence as comparatively eventful, the mild herniation noted 1 time was controlled by lumbar puncture till granulation was complete.

Three weeks after discharge the patient returned to the hospital with increasing left hemiparesis having had on generalized convulsion. There was moderate bulging of the decompression.

A trephine opening as made just posterior to the frontal defect in order to reinspect the subdural space. When the dura was opened normal convolution as seen showing that the subdural abscess had been apparently cured. The wound was closed.

A needle was now inserted through the scalp over the large frontal defect and was passed deeply in several directions. No abscess was encountered.

An encephalogram was made a few days later by the lumbar route which showed displacement of the left lateral ventricle to the left but did not accurately localize the abscess. A few days later ventriculogram was made through left sided trephine opening. This gave definite evidence of large lesion of the right parietal region.

The trephine opening which had been made posterior to the frontal defect previously in order to inspect the subdural space as reopened. A needle was passed downward through the brain substance and to depth of about 3 centimeters, met with an elastic resistance through which the needle was plunged. About 60 cubic centimeters of pus was obtained (Fig. 5) and 8 cubic centimeters of colloidal thorium dioxide instilled. X-ray studies (Fig. 5) revealed large abscess cavity. Six days later the abscess cavity was seen to have increased six by ray. The heavily encapsulated abscess as uncapped and drained. Recovery was uneventful

of the colloidal thorium dioxide. Postoperatively trephine is that used for ventricular oxygen injection. b, Four days later showing increase in size of the abscess which has taken place.

A year later an encephalogram as performed because of few Jacksonian seizures. This showed slight dilatation of the entire ventricular system but no evidence of recurrence.

At the present time this patient feels perfectly well and goes swimming daily.

Here we have the problem of a patient with a large bulging frontal decompression and a suspected subcortical cerebral abscess which might have been anywhere in that cerebral hemisphere. The abscess was finally entered with the exploring needle and outlined with colloidal thorium dioxide. Its exact position and the point at which it lay closest to the surface was determined.

Another case might be briefly mentioned in this connection. A 45 year old doctor entered the hospital in coma with a 3 weeks previous history of otitis media. An encapsulated abscess was tapped through an incision just above and in front of the right ear (Fig. 6). Colloidal thorium was instilled and a small decompression made over where the abscess was thought to be most superficial. Roentgenograms were not taken at this time because of the patient's precarious condition. Subsequent X-ray films showed that this opening had been placed higher than it would have been had films been obtained before decompressing. In spite of this the abscess migrated toward the surface sufficiently within 3 days so that uncapping and drainage were per-

SO CALLED LATERAL ABERRANT THYROID TUMORS

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THE existence in the lateral regions of the neck of cellular masses derived from thyroid tissue has been recognized for more than a hundred years (15), but no serious attempt was made to describe these masses as a separate clinical entity until late in the nineteenth century when isolated reports of cases began to appear in the English and the German literature (1-6).

By 1900, enough cases of these tumors had been reported to give rise to speculation concerning the origin and the pathological characteristics of the growths. There was evidence to indicate that the thyroid gland originated from two separate anlagen, an unpaired median component and paired lateral components, which fused early in fetal life. The earliest school of thought, and by far the largest one today, attempted to explain the origin of "lateral aberrant thyroids" by some abnormality in the development of the lateral anlagen. Schrager, in 1906, expressed the belief that these masses were essentially benign tumors arising as a hyperplasia of normal thyroid elements detached from the lateral anlagen before fusion, in response to an increased demand for thyroxin created by subefficient function of the thyroid proper.

The predominantly papillary nature of these tumors and their frequent association with similar tumors in the corresponding thyroid lobe were first pointed out by Low in 1903. He emphasized that their rate of growth was slow and that metastasis to distant regions was rare, spread tending to occur rather by local invasion of the lymph channels. Many years later Billings and Paul reiterated these observations. The peculiar structure of these tumors led to the belief that "lateral aberrant thyroids" were derived not from normal thyroid elements but from tissue which was constitutionally inferior to that of the thyroid proper.

Kingsbury demonstrated that the lateral anlagen degenerated after fusion with the median anlage and probably disappeared completely. Leech, Smith, and Clute and, later, Cattell expressed the belief that "lateral aberrant thyroids" originated from fetal rests derived from the degenerated lateral anlagen and were intrinsically malignant. They concluded that the frequently

coexistent papillary tumor in the corresponding thyroid lobe arose from a fetal rest derived from the same source. Crile (7,8) concurred in their explanation of the origin of thyroid and "aberrant" tumors, but expressed the opinion that these tumors were remarkably benign in their behavior.

In 1931 Dunhill revived Schrager's conception of the physiological stimulus concerned in the genesis of "lateral aberrant thyroids." He expressed the belief that the lateral anlagen were constitutionally inferior to the median anlage and that tissue derived from them, whether situated within or without the thyroid lobe, was prone to undergo papillary change in response to stimulation by ordinary physiological demands. Thus arose the theory of "activated rests." Van den Wildenberg expressed the belief that the papillary cystadenomas so formed were precancerous and that further stimulation by relative thyroid insufficiency caused them to become malignant.

Gretelman and Russum extended this idea to account for recurrences, stating that continuation of the stimulus caused other tiny and previously unaffected rests, missed at the first operation, to develop into palpable tumors. They suggested that the thyroid itself be explored because it frequently is involved by a similar tumor.

In 1940 Ward further elaborated the theory of "activated rests." He, like Dunhill, expressed the belief that stimulation of any tissue derived from the lateral anlagen resulted in papillary change, however, he was of the opinion that this change, occurring among children, was in a reversible stage and would regress if the stimulus were removed by treatment of the patients with iodine, whereas, among adults, owing to the loss of some cancer-resisting factor, the process became irreversible and went on to malignancy. Thus he advocated radical surgical procedure and radiation in the treatment of adults. Cohn and Stewart, in the same year, stated the belief that the location of a papillary tumor within or without the lateral thyroid lobe depended on whether embryonic tumor cells were split off the lateral component before or after fusion took place. If this splitting off occurred both before and after fusion, coexistent primary tumors appeared in the thyroid and side of neck. They stressed importance of complete excision of tumor to prevent recurrence.

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15.800 and the temperature was 99 degrees. A diagnosis was made of abscess of the left cerebral hemisphere, metastatic from the lung rather than secondary to the otitis media which in my experience so rarely causes abscess in infants.

A needle was passed through the left side of the anterior fontanelle to a depth of about 3 centimeters. On withdrawing the stylet 45 cubic centimeters of pus was obtained, following which 15 cubic centimeters of colloidal thorium dioxide as injected (Fig 7).

X ray studies, to our great surprise, revealed the contrast medium to be in the left subdural space. By means of two large trephine openings, one in the frontal and one in the parietal region, the subdural space was entered. There was a purulent membrane attached to the inner surface of the dura. There was a heavy inner membrane apparently holding the brain down. Several incisions were made into the latter but it was soon obvious that removal of much of this membrane was out of the question. Specimens of both membranes were taken for pathological examination. All type rubber tissue drains were placed in the subdural space.

The infant now made an amazing improvement. The drains were removed on the sixth postoperative day. He was discharged with the incisions completely healed, 7 weeks later.

Pathological examination of the membranes revealed that infection had developed in what had undoubtedly been a chronic subdural hematoma. Culture of the pus obtained at operation showed *Staphylococcus aureus*.

On examination five months later the child could still not sit up alone but noticed things and was making an effort to use both upper extremities. It has been impossible to contact the family since that time.

The advantage of using a contrast medium which mixed freely with the contents of a purulent cavity is obvious in this case. The operator had thought that he was dealing with an intracerebral abscess until the x ray studies were obtained.

CONCLUSIONS

1. Colloidal thorium dioxide can be used to advantage in outlining cystic tumors of the cerebral hemispheres. This not only gives a

due to the pathological nature of the neoplasm but simplifies the surgical approach should operation be deemed advisable.

2. This contrast medium is of value in the treatment of the encapsulated abscess of the brain whether it be dealt with by repeated tapping after the method of Dandy open drainage or complete excision as performed by Vincent.

3. Colloidal thorium dioxide has the advantage over iodized poppy seed oil or air in that it mixes readily with fluid contents and may be phagocytized by the surrounding wall of an abscess so that the capsule itself will be visible in the roentgen-ray within 3 days or less.

4. There can be little danger in the use of colloidal thorium dioxide from the effect of long standing radioactivity since the main mass of this substance is removed in the evacuation of the cavity.

5. It is suggested that there might be wider application in the field of general surgery as in visualization of an empyema cavity. In the drainage of a thoracic empyema, the difficulty increases as the cavity becomes smaller. It is at this later stage that the colloidal thorium dioxide which has been phagocytized by the empyema wall might show when obliteration is complete.

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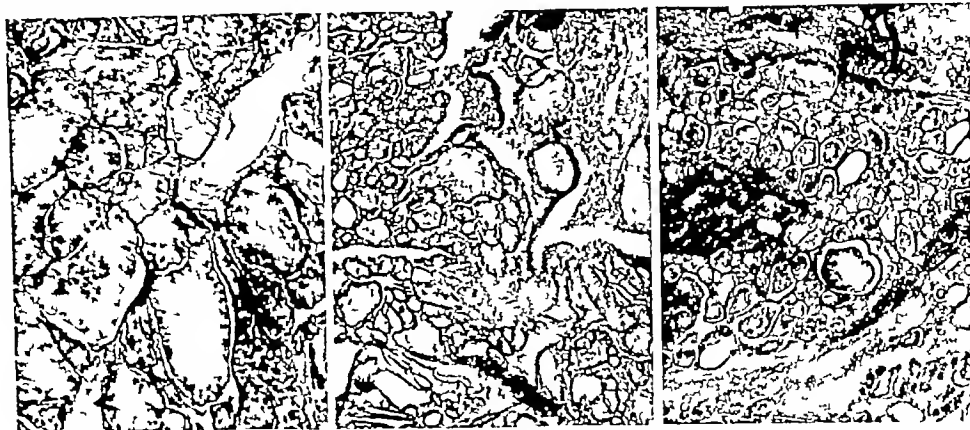


Fig 1

Fig 2

Fig 3

Figs 1, 2, and 3 Lateral aberrant thyroid tumors in the 3 cases in our series in which the growths were benign. Sections from all three are indistinguishable from sections of colloid adenoma.

died of carcinoma of the thyroid gland subsequent to removal or biopsy of a malignant "aberrant thyroid", in 4 cases the survival period varied from 11 to 19 years. One patient lived for 9½ years subsequent to the appearance of pulmonary metastatic lesions a year after removal of the "aberrant thyroid". It is apparent, therefore, that malignant "aberrant thyroids" are very slow-growing on the average, but that they eventually may cause death.

Of the 54 patients 3 had "lateral aberrant thyroid tumors" which, on microscopic examination, proved to be benign (Figs 1, 2, and 3). In 2 of these cases a large, nodular goiter was associated with the "aberrant" thyroid tumor, which in each instance was situated immediately above one or the other superior thyroid pole. In the third case, the "aberrant" tumor was situated at the angle of the jaw on the right side and had been present for 30 years without change in its size. There was no direct connection between the thyroid tumor and the "aberrant" tumor in any of the 3 cases, in each case, microscopic examination revealed that tumors were composed of colloid and fetal adenomatous thyroid tissue without evidence of cellular undifferentiation, mitosis, vascular invasion, or lymphoid tissue.

The 51 other "aberrant" thyroid tumors on microscopic examination proved to be malignant. In 31 cases, 60 per cent, there was an associated tumor of the thyroid, the malignant nature of which was confirmed by microscopic examination, by obvious inoperability, or by subsequent death of the patient from carcinoma of the thyroid. In each of these 31 cases the thyroid tumor and the "aberrant" tumor were on the same side of the

neck, and in each of 19 of these cases in which specimens from both tumors were obtained, the structure of the tumors was histologically identical (Figs 4 to 9). All of the 10 deaths in the series of 54 cases occurred in this group, and of 24 patients who experienced recurrence of tumor, 19 had both thyroid and "aberrant" tumors.

Of the 20 patients remaining, 3 had associated thyroid tumors, the pathological nature of which was doubtful clinically and was not determined by operation. In the 17 other cases clinical evidence of thyroid tumor was not observed, in 13 of these cases, attempt was not made to examine the thyroid at operation, but in 4 the gland was exposed and, since it seemed normal on palpation, was left undisturbed by the surgeon. In the whole group of 20 cases, recurrence took place in 4, of which 1 was in the group of 4 in which the thyroid gland was left undisturbed at operation. The thyroid gland was not involved later in any case, nor was death related to the disease in any case. At the time this paper was written 10 patients were living and free from recurrence of tumor, 4 had had one recurrence, 1 died of natural causes, reports were not received from the 5 others after dismissal.

In 38 of the 51 cases of malignant tumor, 75 per cent, the pathologist on examination of the "aberrant" tumor made a diagnosis of papillary adenocarcinoma. Of these tumors, 20 were classified as of grade 1, 18 as of grade 2, the grading was on a basis of 1 to 4, in which grade 1 is the least malignant and grade 4 the most malignant. In 12 of the tumors of grade 2 the papillary tissue was mixed with nonpapillary, solid carcinomatous tissue. The tumors of grade 1 were distinguished by the long, arborizing processes which projected from

A second school of thought, much in the minor it held that lateral aberrant thyroids were metastatic carcinomas in the cervical lymph nodes secondary to primary carcinoma of the corresponding thyroid lobe. Wohl, in 1917, advised thinking of this possibility when a so-called lateral aberrant thyroid was found and Eberts, in 1933, advocated removal of the corresponding thyroid lobe even though it appeared normal. It was pointed out by one of us (J. deJ. P.) in 1934 (25) and again in 1939 (26) that these lateral masses, incorrectly termed "lateral aberrant thyroids," were in reality true metastatic carcinomas.

A few other investigators explained the origin of these tumors as nests of normal thyroid cells which either occupied their aberrant position because of natural distribution (31, 35) or were dragged away from the thyroid proper by muscles, vessels and nerves which were developing (9, 23, 37).

George Crile, Jr. in two recent papers, swung back to the opinion held by Schurager that these were benign tumors. Crile stated that papillary tumors of the thyroid gland, in his experience, did not metastasize to lymph nodes and that lateral aberrant thyroids were not metastatic carcinomas and were not as a rule malignant. He expressed the opinion that the finding of a hard, palpable tumor in the thyroid gland, together with multiple nodules in the neck, was confirmatory evidence of the presence of lateral aberrant thyroid tumor. He expressed the belief that because these tumors were benign and did not spread, because they did not recur after operation for their removal, and because they never caused the death of the patient, complete cure would result provided they were removed completely.

Since 1920 the microscopic diagnosis of malignant disease in thyroid tissue has received much attention. Graham (1) stated the belief that capsular invasion was the main criterion in the diagnosis of the nonpapillary type of cancer that capsular invasion and lymphatic invasion were the criteria in the purely papillary types. Ward and others (22) stated that capsular invasion and lymphatic and vascular invasion were the only reliable signs of malignant change. Neither Ward nor Crile believed that the presence of lymphoid tissue in an "aberrant thyroid" was a sign that the tumor was a metastatic lesion in a lymph node. However, Broders (3, 4) expressed the opinion that the most reliable signs of malignancy were cellular undifferentiation and mitoses.

A. LIST OF FIFTY-FOUR CASES

In the selection of cases at the clinic to correspond with those described by other writers, all

those were chosen first in which a benign or a malignant tumor of thyroid tissue was discovered in the lateral region of the neck, without any gross connection with the thyroid gland itself. This group included cases in which the lateral cervical tumor had been removed elsewhere prior to the patient's visit to the clinic and other cases in which it had been removed or in which biopsy had been made at some time after operation on the thyroid gland. In many cases there had been also a tumor in the thyroid itself before or at the time of or after operation on the cervical tumor. The whole group was divided into two series: the first series, 54 cases, included only cases in which the lateral cervical tumor was the patient's main complaint or as the main reason for performing the operation. In these cases the cervical tumors were considered "lateral aberrant thyroid" irrespective of the presence of a thyroid tumor. In all the other cases there were malignant tumors of the thyroid gland which were themselves the reason for operating and the associated lateral cervical tumors were unquestionably, in our opinion, regional metastatic lesions. In 5 cases of the second series the cancers were papillary; microscopic analysis of these cancers was made for comparison with the tumors in the first series of cases.

Of the 54 patients in the first series, 29 were females and 25 were males. The highest age incidence occurred in the fourth decade among the former. In the third decade among the latter. The clinical diagnosis most commonly made was of tuberculous adenitis in those cases in which thyroid tumor was not present, carcinoma of the thyroid with metastatic extension in those in which thyroid tumor was present. In many of the latter cases, a double diagnosis was made of adenomatous goiter together with cervical adenopathy, lymphoblastoma, adenitis, and so forth. In 16 cases there were symptoms of pressure on surrounding tissue but they were not of help in arriving at correct diagnosis.

The "aberrant thyroid" tumor consisted of multiple nodules in 36 of the 54 cases, and of a single mass in 18. The growth was situated deep to one or the other sternocleidomastoid muscle in 50 per cent, in the posterior triangle of the neck in 27 per cent, in the submandibular triangle in 19 per cent, and in the carotid triangle in the remainder of the cases. Before operation, the average duration of the tumor had been 5 years; the duration exceeded 10 years in 7 of the cases in which the lesion was malignant. Recurrence of the tumor usually took place from 6 months to 1 year after operation, but in 5 cases there was a delay of more than 5 years. Ten patients, 18.5 per cent,



Fig 10

Fig 11



Fig 12

Fig 13

Figs 10 to 13 Histological evidence of malignancy in lateral aberrant thyroid tumors, tumor thrombus in a capsular vein (Fig 10), capsular lymphatic distended by tumor tissue (Fig 11), typical lymph node structure with carcinomatous metastasis (Fig 12), tumor cells lying in a peripheral sinus of a lymph node (Fig 13)

marked. The tumors of grade 4 invaded all the tissues surrounding them, as would be expected.

Twenty-eight, 55 per cent, of the malignant "aberrant" tumors contained lymphoid tissue, usually in the form of a shell around the cancerous tissue with finger-like processes extending into it (Fig 12). Often peripheral sinuses were seen between lymphoid tissue and capsule, at times these contained cancer cells (Fig 13). Only one of the thyroid tumors contained lymphoid tissue.

The operative procedures used in the treatment of these 54 patients are given in Table I.

An analysis of the results was made, from the standpoint of recurrence of tumor, according to the completeness of the operative procedure, and as to whether or not postoperative treatment by radiation was given. Removal of all grossly involved structures, including the corresponding thyroid lobe if it, too, was involved, constituted a complete procedure. Of 21 cases in which complete removal of the tumor was followed by radiation, recurrence took place in 8, or 38 per cent. In 16, in which removal was incomplete but was followed by radiation, recurrence took place in 10, or 62.5 per cent. In 12 cases of complete removal,

without radiation, recurrence took place in 5, or 42 per cent, an incidence equal to that in the first group. Therefore, among those patients who received postoperative treatment by radiation, complete removal of the grossly involved structures,

TABLE I—OPERATIVE TREATMENT OF SO CALLED ABERRANT THYROID GLANDS

	Cases
1 Excision of aberrant thyroid tumor	17*
2 Dissection of lymph nodes of neck	
Partial	3*
Radical	4
3 Hemithyroidectomy combined with	
Excision of aberrant thyroid tumor	4
Dissection of lymph nodes, partial	3
Dissection of lymph nodes, radical	2
4 Removal of specimen of aberrant thyroid	11
5 Total and subtotal thyroidectomy with	
Excision of aberrant thyroid tumor	3
Dissection of lymph nodes, radical	3†
6 Hemithyroidectomy subsequent to excision of aberrant thyroid tumor or dissection of lymph nodes	3
7 Removal of thyroid isthmus	1†
Total	54

*In one case in each group hemithyroidectomy was done before patient came to clinic.

†In one case biopsy of aberrant thyroid tumor was performed before patient came to clinic.



Fig. 4



Fig. 5



Fig. 6



Fig. 7

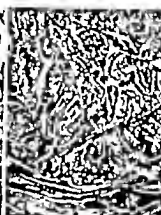


Fig. 8

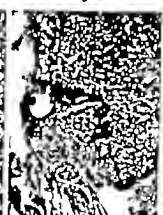


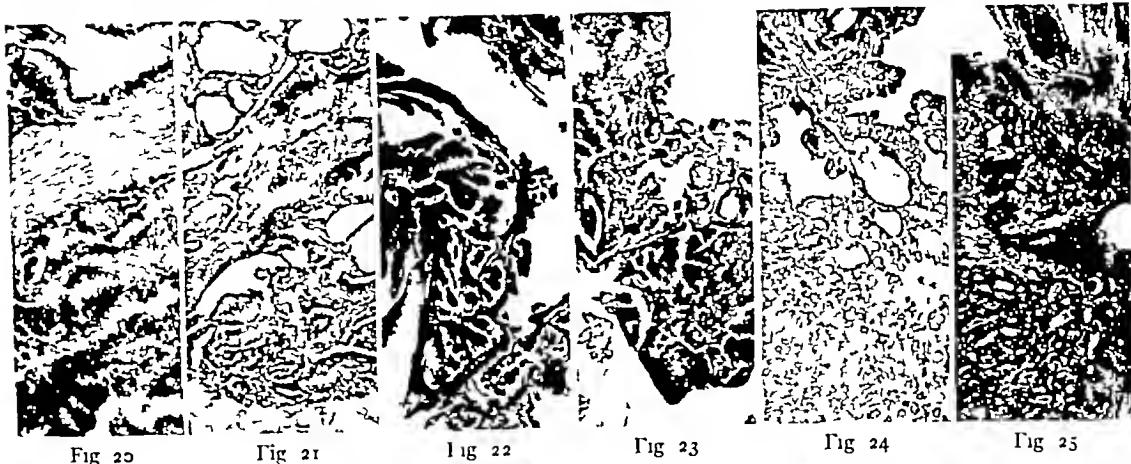
Fig. 9

FIGS. 4 TO 9. The pathological characteristics of papillary lateral aberrant thyroid tumors (Figs. 4, 5, and 6) and of the tumors in the corresponding thyroid lobe compared (Figs. 7, 8, and 9). Papillary adenocarcinoma, grade (Figs. 4 and 7) pure papillary adenocarcinoma, grade (Figs. 5 and 8) mixed papillary and nonpapillary adenocarcinoma, grade (Figs. 6 and 9).

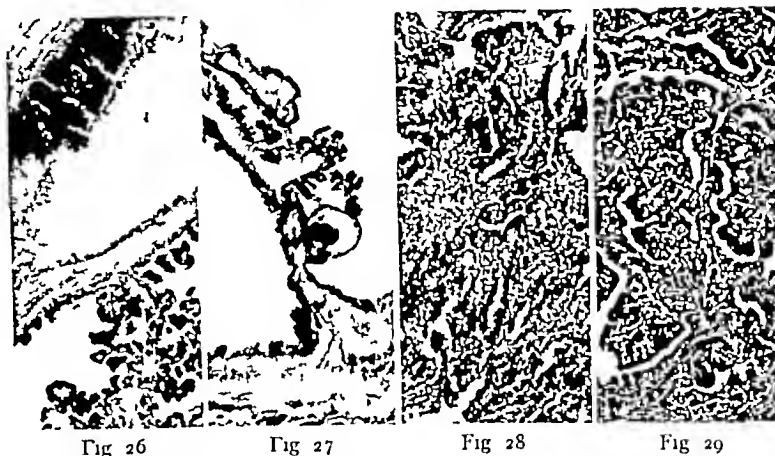
thin cystic walls into large spaces, the lining epithelium being one layer thick. In the most part in the tumors of grade 2 the processes were thick and stubby, were covered by two or more layers of epithelial cells, and usually projected into small cystic spaces which often were surrounded by sheets of less well-differentiated cancer cells. Evidence of mitosis was present in all specimens of the papillary group and was observed more frequently in the tumors of grade 2. Prolonged search was required to discover mitotic figures in the majority of tumors of grade 1. Vascular invasion could not be demonstrated in any tumor of grade 1 and in only a few of the tumors of pure grade 2, but in the majority of the tumors in association of the capsule or the capsular lymphatics was evident. The majority of the tumors of mixed grade 2 revealed vas-

cular capsular and lymphatic invasion (Figs. 9, 11).

The 3 other malignant aberrant tumors are nonpapillary adenocarcinomas and all are associated with thyroid tumors. They were graded from 1 to 4 according to the degree of cellular undifferentiation, the tumors of grade 4, or diffuse carcinoma, being totally undifferentiated. Evidence of mitosis was extremely difficult to find in the tumors of the first three grades but was abundant in those of grade 4. Invasion of the capsule was discovered in all the tumors of higher grade and in most of those of grade 2 but was lacking in some of the tumors of grade 2 and of grade 1. Capsular and lymphatic invasion was less prominent in the tumors of this group than in those of the papillary group, but nevertheless as well



Figs 20 to 29. Lateral aberrant thyroid tumor (Figs 20, 22, 24, 26, and 28) and the tumor of the corresponding thyroid lobe (Figs 25, 26, 27, 28, and 29) compared in 3 cases (Figs 20 and 21, 22 and 23, 24 and 25) in which the thyroid tumor was discovered by the pathologist after its removal, and in 2 other cases (Figs 26 and 27, 28 and 29) in which it was discovered by the surgeon at operation

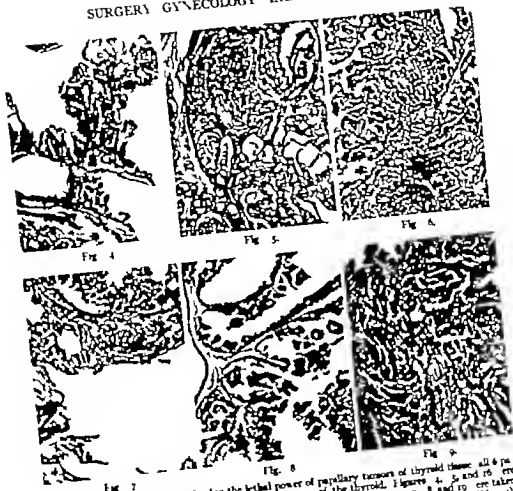


nosis, we found that the metastatic nodes, if not bilateral, were always on the same side as the involved thyroid lobe and that their histological structure invariably was identical with that of the thyroid carcinoma. There was definitely lymphoid tissue surrounding the malignant regions in 9 of the 15 representative metastatic nodules, 60 per cent, an incidence which compares almost exactly with that in the series of so called lateral aberrant thyroid tumors. Lymphoid tissue was present in the thyroid tumors in 2 cases. Vascular invasion was evident in 1 of the 7 tumors of grade 1 and in 7 of the 8 tumors of grade 2. The frequency of mitosis and of capsular and lymphatic invasion closely approximated that of "aberrant thyroid" tumors.

It is obvious, therefore, that the cases of the 2 series are indistinguishable from one another pathologically and that the separation out of some of the tumors as examples of "lateral aberrant thyroid tumor" was purely empirical according to the relative degree of prominence of the clinical his-

tory and findings of the "aberrant" or the thyroid tumor. The frequent insignificance of the associated thyroid tumor is illustrated by the fact that in 4 cases the thyroid tumor was not discovered until the gland was exposed at operation, in 3 others, the surgeon removed the homolateral thyroid lobe, even though it looked and felt normal, because the pathologist's report of the excised cervical tumor was papillary adenocarcinoma of the thyroid type, and in each a tiny and identical tumor was found buried inside the lobe. In no case in which the homolateral lobe was removed did the pathologist fail to find in that lobe a tumor identical in structure with that of the "aberrant thyroid." The following report of cases serves to illustrate the points mentioned in this paragraph.

CASE 1 (Figs 20 and 21) A man, aged 32 years, who came to the clinic complaining of dysphagia, had had two tumors, one under the right sternocleidomastoid muscle and one at the angle of the jaw, for 10 years. In the 5 months previous to admission he had noticed rapid increase in size of the masses. A clinical diagnosis of Hodgkin's disease



Figs. 4-9. Evidence confirming the lethal power of papillary tumors of thyroid tissue: all 6 patients represented in Figures 4-9 died of carcinoma of the thyroid. Figures 4, 5, and 6 are taken from the "lateral aberrant" thyroids in cases in the first series. Figures 7, 8, and 9 are taken from the thyroid tumors of patients in the second series. Papillary adenocarcinoma, grade (Fig. 4) pure papillary adenocarcinoma, grade (Fig. 5) mixed papillary and nonpapillary adenocarcinoma, grade (Fig. 6) pure papillary adenocarcinoma, grade (Fig. 7, 8, and 9) of the type commonly called benign papillary cystadenoma.

both thyroid and aberrant thyroid afforded a better prognosis for cure. All of the deaths occurred in the group in which the surgical procedure was incomplete in spite of the fact that recurrence developed in 4 per cent of the cases in which removal was complete. Recurrence took place in 5 of the 38 cases of thyroid tumor (40 per cent) and in 9 of the 30 cases of papillary tumor (70 per cent). Of the 30 cases in the latter group, 2 were caused by metastases in the papillary group. Thus it becomes clear that although the papillary tumors are clinically much more powerful than the nonpapillary, their power

to cause death cannot be questioned even when nonpapillary carcinomatous elements are lacking. Confirmatory evidence is furnished by the photomicrographs in Figures 17, 18 and 19. Treatment by radiation would seem to be of questionable value unless the surgical procedure was "complete" and even then it is not strikingly effective.

ANALYSIS OF 15 CASES OF PAPILLARY CARCINOMA OF THYROID WITH REGIONAL METASTASES AND COMPARISON WITH CASES OF ABERRANT TUMOR

Comparing with the cases in the series described previously those 15 cases in which papillary carcinoma of the thyroid with regional metastatic extension was conceded to be the correct diag-

frequent mitotic figures and showed capsular invasion, lymphoid tissue was not found. The thyroid tumor was composed of mixed solid and cystic tissue, contained many mitotic figures, and gave evidence of vascular, capsular, and lymphatic invasion.

Six months later the patient was subjected elsewhere to right radical block dissection of tumors of the neck and afterward was treated by radiation. Seven years after her first operation she reported that she was in good health, free from recurrence.

CASE 3 (Figs 24 and 25) A woman, aged 37 years, came to the clinic because of gradually increasing tumor of 4 years' duration situated under the right sternocleidomastoid muscle. Clinical diagnosis was made of cervical adenopathy, and the tumors were excised. The pathologist reported that the growths were papillary carcinoma. Although the thyroid on surgical exploration apparently was normal, the surgeon was doubtful and resected the right lobe, in the upper pole of which were found two small nodules that proved to be carcinomatous. Microscopic study revealed mixed papillary and nonpapillary adenocarcinoma, grade 2, of the thyroid with regional metastatic extension. Patient received radiation treatment.

Five months later the patient returned with recurrence of tumors under the right sternocleidomastoid muscle. Radical block dissection was made and was followed by radiation. The pathologist's report was identical with that made 5 months previously. The "aberrant" tumor was solid, contained abundant mitotic figures and evidence of vascular invasion, lymphoid tissue was not present. The thyroid tumor was of the same type but in addition showed evidence of capsular and lymphatic invasion. The recurrent tumor which was removed at the second operation possessed all the features of both the "aberrant" tumor and the thyroid tumor and contained lymphoid tissue.

Nine years after first operation the patient living and well.

CASE 4 (Figs 26 and 27) A man, aged 24 years, had had multiple tumors of the right side of the neck, under the sternocleidomastoid muscle and at the angle of the jaw, for 10 years. They gradually had increased in size. When operation was performed for excision of the tumors, surgical exploration of the thyroid revealed a tumor in the right lobe, and right hemithyroidectomy was done. The pathologist reported papillary adenocarcinoma, grade 1, of the thyroid with regional metastatic extension. Both the thyroid tumor and the metastatic tumors were cystic and contained occasional mitotic figures, lymphoid tissue was present, and there was evidence of capsular and lymphatic invasion. The papillary carcinoma arose from an adenoma. The lymphoid tissue in the thyroid was a nodule extrinsic to the encapsulated tumorous tissue and was not invaded by it. Patient later received treatment by radiation.

Eight years afterward the patient returned to the clinic because of recurrence of tumors under the left sternocleidomastoid muscle, he again received treatment by radiation. Two years later it was reported tumors were still present. The patient did not return for further treatment.

CASE 5 (Figs 28 and 29) A woman, aged 22 years, came to the clinic because of multiple tumors of the neck and at the angle of the jaw on the right side. The growths had been present for 2 years and gradually were increasing in size. Physical examination revealed that the tumors in the neck were under the sternocleidomastoid muscle. Diagnosis was made of tuberculous adenitis. Biopsy at the time of surgical intervention revealed the presence of papillary carcinoma, a right radical block dissection of the tumors was made and after exploration of the thyroid, the right lobe which was enlarged slightly, was removed.

The pathologist reported papillary and nonpapillary carcinoma, grade 2, of the thyroid with regional metastatic

extension. The specimen of tissue removed for biopsy was solid and, on microscopic examination, was found to contain occasional mitotic figures. The thyroid tumor and metastatic tumors were solid and mitotic figures were present with evidence of capsular, vascular, and lymphatic invasion. None of specimens contained lymphoid tissue.

Subsequent to operation the patient received treatment by radiation. Two months afterward recurrence of tumors had not taken place.

CASE 6 (Figs 4 and 7) A girl, aged 18 years, registered because of the presence for 9 months of multiple tumors on the left side of the neck. On physical examination the growths proved to be under the left sternocleidomastoid muscle and in the left posterior triangle. Three weeks before the patient came to the clinic, biopsy had been performed elsewhere of one of tumors in posterior triangle and pathologist's report papillary carcinoma.

A clinical diagnosis was made of cervical carcinoma and at operation all the cervical nodules were removed. The thyroid was examined and apparently was normal. The pathologist reported the nodules as papillary adenocarcinoma, grade 1, probably metastatic from the thyroid. Treatment by radiation was not given.

The patient returned 1 month later with a recurrence under the left sternocleidomastoid muscle and a palpable tumor in the left lobe of the thyroid. Left radical block dissection and left hemithyroidectomy were done. Both tumors proved to be papillary adenocarcinoma, grade 1, identical with the nodules removed earlier. Microscopic examination of the "aberrant" tumor revealed solid tissue that contained occasional mitotic figures, lymphoid tissue was present and capsular invasion had taken place. The findings in thyroid tumor and metastatic nodes were the same except thyroid tumor contained no lymphoid tissue.

The patient received treatment by radiation, 9 months later she had remained free from signs of recurrence.

In 9 cases, the thyroid tumor did not become clinically detectable until some time after removal of or biopsy of the "aberrant" tumor, in 3, the thyroid tumor was the first to appear. In 17 cases, as has been stated, a tumor in the thyroid gland never developed, even though there was recurrence of the "aberrant" tumor in the neck. As but 4 of the 17 patients received radiation and by this treatment a primary growth in the thyroid may have been destroyed. Believing, as we do, that all "lateral aberrant thyroids" are metastatic tumors from primary growths in the thyroid, the failure of appearance of a thyroid tumor in the last 4 cases must be attributed to the slow rate of growth which has been shown to characterize this type of carcinoma.

EVALUATION OF STUDY

It has been pointed out previously herein that some of the authors who believe in the "activated rest" theory of origin of "lateral aberrant thyroids" have expressed the opinion that physiological overstimulation of the constitutionally inferior tissue derived from the lateral anlage causes to develop in that tissue papillary change which proceeds to malignancy. These men accept the view that the lateral components do form part



Fig. 30



Fig. 31



Fig. 32



Fig. 33



Fig. 34



Fig. 35

Figs. 30 to 35. Histological and roentgenological evidence of distant metastases from pure and mixed papillary tumors of thyroid tissue. Fig. 33 shows metastatic involvement of the skull by papillary adenocarcinoma, grade. Figures 30, 31, and 32 show metastases to the mediastinum, to the lungs, and to the lungs, respectively.

from mixed papillary and nonpapillary adenocarcinoma, grade. Figure 34, metastasis to the lungs from nonpapillary adenocarcinoma, grade. 35b papillary elements. Figure 35, histological section of scalp nodule secondary to pure papillary adenocarcinoma, grade. (Figures 30, 31, 32, 33 all represent so-called lateral aberrant thyroid tumors.)

as made and operation as performed for excision of the tumors, the thyroid was not examined surgically. The pathologist at first reported that the tumors were bronchial cystadenomas but later changed diagnosis to papillary adenocarcinoma, grade. Treatment by radiation not given.

The patient returned 9 months later with recurrence under the right sternocleidomastoid muscle and at the angle of the jaw on the right and on the left side. Right partial block dissection as done. The pathologist reported that the tumors were adenocarcinoma, grade, probably metastatic from the thyroid. Although the thyroid felt and looked normal, because of the pathologist's diagnosis of adenocarcinoma, the right lobe was resected. Macroscopic examination revealed in the lower pole a tiny nodule of meaty looking tissue which proved to be papillary carcinoma, grade. The nodule at the angle of the jaw on the left side was not removed. The "aberrant" tumor as cystic, contained lymphoid tissue and mitotic figures were evident. The thyroid tumor as solid and there were occasional mitotic figures. The metastatic lesions were cystic giving evidence of capsular and lymphatic invasion, and con-

tained lymphoid tissue. All the growths were simple papillary carcinomas arising in adenomas, except, in the metastatic nodes, for occasional regions which were suggestive of nonpapillary adenocarcinoma.

The patient received treatment by radiation. Two months later recurrence had not taken place.

CASE (Figs. 36 and 37). A woman aged 37 years, on examination at the clinic had had a single tumor under the right sternocleidomastoid muscle for 6 months. The patient stated that the tumor fluctuated in size and that when it was large it caused dyspnea by pressure on the trachea. A diagnosis of bronchial cyst was made clinically and operation as performed for removal of the growth. The thyroid appeared normal on surgical exploration, but because of the pathologist's report that the cyst was papillary carcinoma, right hemithyroidectomy as done and in the extreme tip of the superior pole of the lobe there was found a tiny nodule of carcinomatous tissue. Macroscopic examination of the specimen revealed mixed papillary and nonpapillary carcinoma, grade, of the thyroid, with typical metastatic lesions. The cervical cystic tumor contained

frequent mitotic figures and showed capsular invasion, lymphoid tissue was not found. The thyroid tumor was composed of mixed solid and cystic tissue, contained many mitotic figures, and gave evidence of vascular, capsular, and lymphatic invasion.

Six months later the patient was subjected elsewhere to right radical block dissection of tumors of the neck and afterward was treated by radiation. Seven years after her first operation she reported that she was in good health, free from recurrence.

CASE 3 (Figs 24 and 25) A woman, aged 37 years, came to the clinic because of gradually increasing tumor of 4 years' duration situated under the right sternocleidomastoid muscle. Clinical diagnosis was made of cervical adenopathy, and the tumors were excised. The pathologist reported that the growths were papillary carcinoma. Although the thyroid on surgical exploration apparently was normal, the surgeon was doubtful and resected the right lobe, in the upper pole of which were found two small nodules that proved to be carcinomatous. Microscopic study revealed mixed papillary and nonpapillary adenocarcinoma, grade 2, of the thyroid with regional metastatic extension. Patient received radiation treatment.

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Nine years after first operation the patient living and well.

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Subsequent to operation the patient received treatment by radiation. Two months afterward recurrence of the tumors had not taken place.

CASE 6 (Figs 4 and 7) A girl, aged 18 years, registered because of the presence for 9 months of multiple tumors of the left side of the neck. On physical examination the growths proved to be under the left sternocleidomastoid muscle and in the left posterior triangle. Three weeks before the patient came to the clinic, biopsy had been performed elsewhere of one of tumors in posterior triangle, and pathologist's report papillary carcinoma.

A clinical diagnosis was made of cervical carcinoma and at operation all the cervical nodules were removed. The thyroid was examined and apparently was normal. The pathologist reported the nodules as papillary adenocarcinoma, grade 1, probably metastatic from the thyroid. Treatment by radiation was not given.

The patient returned 1 month later with a recurrence under the left sternocleidomastoid muscle and a palpable tumor in the left lobe of the thyroid. Left radical block dissection and left hemithyroidectomy were done. Both tumors proved to be papillary adenocarcinoma, grade 1, identical with the nodules removed earlier. Microscopic examination of the "aberrant" tumor revealed solid tissue that contained occasional mitotic figures, lymphoid tissue was present and capsular invasion had taken place. The findings in thyroid tumor and metastatic nodes were the same except thyroid tumor contained no lymphoid tissue.

The patient received treatment by radiation, 9 months later she had remained free from signs of recurrence.

In 9 cases, the thyroid tumor did not become clinically detectable until some time after removal or biopsy of the "aberrant" tumor, in 3, the thyroid tumor was the first to appear. In 17 cases, as has been stated, a tumor in the thyroid gland never developed, even though there was recurrence of the "aberrant" tumor in the neck. All but 4 of the 17 patients received radiation and by this treatment a primary growth in the thyroid may have been destroyed. Believing, as we do, that all "lateral aberrant thyroids" are metastatic tumors from primary growths in the thyroid, the failure of appearance of a thyroid tumor in the last 4 cases must be attributed to the slow rate of growth which has been shown to characterize this type of carcinoma.

EVALUATION OF STUDY

It has been pointed out previously herein that some of the authors who believe in the "activated rest" theory of origin of "lateral aberrant thyroids" have expressed the opinion that physiological overstimulation of the constitutionally inferior tissue derived from the lateral anlagen causes to develop in that tissue papillary change which proceeds to malignancy. These men accept the view that the lateral components do form part

of the lateral thyroid lobes. In support of their opinion, they state further that carcinoma seldom, if ever, occurs along tract of median anlage.

It is well recognized that among adolescents physiological overstimulation of the thyroid in the presence of iodine deficiency results in diffuse colloid goiter. Goiter of this type is devoid of any of the papillary elements which one would expect to find, according to these writers, if the lateral anlagen were constitutionally inferior. Furthermore papillary carcinoma of the thyroid gland often involves a whole lobe uniformly commonly stopping abruptly at the midline. Thus both median and lateral components are in a way similarly the line of demarcation appearing to be based on direction of lymph flow. Probst and Agnew reported a case of papillary change in a nodule of thyroid tissue situated in the right side of the base of the tongue the position of this nodule would indicate that it was derived from the median component. Such a case offers proof that papillary change is not limited to tissues derived from the lateral anlagen.

We have shown that the majority of the so called lateral aberrant thyroids occupy positions in the neck anatomically identical with the deep cervical lymph nodes and that 55 per cent of them present definite microscopic evidence of lymph nodal tissue that is, in capsule lymph follicles and peripheral sinuses (Figs. 2 and 13) which have not been entirely destroyed by the malignant cells. It has been pointed out that some observers have expressed the opinion that such tissue is not indicative of metastatic infection of a lymph node but is characteristic of lateral aberrant thyroid tissue. Yet in our series of cases we were unable to find any evidence of lymph nodal tissue in the thyroid tumors which, according to the same men are derived from the same source as the aberrant thyroids. Furthermore photomicrographs of the developing median and lateral anlagen at the stage of budding out from the pharynx, reveal no lymphocytes associated with the thyroid epithelial primordium (34). In our opinion, it is impossible to distinguish microscopically metastatic lymph nodes from aberrant thyroids in the same or in different cases.

Tumors derived from the median anlage are found at its site of origin or along the path of its descent. If lateral aberrant thyroid tumors were really derived from the lateral anlagen, one would expect to find them situated also somewhere along the tract of the lateral anlagen from the pharyngeal wall to the thyroid. Weller showed that this tract lies between the carotid sheath and the thyroid lobe laterally and the trachea and esophagus

medially. We have found that the majority of these lateral aberrant tumors lie superficial to or external to the carotid sheath. There is no record at the clinic of the finding of normal thyroid tissue elements lateral to the thyroid gland during the course of the routine microscopic examination of material removed in several thousand radical dissections of the neck performed for good reasons other than cancer of the thyroid gland.

Lahey and others expressed the belief that the papillary thyroid tumors coexistent with many lateral aberrant thyroids are metastatic from the latter into the thyroid. Mahomed and others showed that the direction of the flow of lymph in the thyroid gland is outward from the gland to the deep cervical nodes, the lymphatics of each lobe going to the nodes of their own side and not crossing over to the opposite side. In our experience metastatic tumors discovered in the thyroid gland invariably have been blood borne most commonly from a hypernephroma (37). Carcinomas of the tongue lips, pharynx, and so forth characteristically invade the cervical nodes but have rarely if ever been found to metastasize to the thyroid.

Because of the unusually slow growth in many instances, the contention has been made that these lateral aberrant papillary tumors are not malignant that recurrence does not take place subsequent to their surgical removal that they do not give rise to distant metastatic growths, and that they do not cause death. We believe that we have presented data that are convincing evidence that these low grade lateral aberrant thyroid tumors spread more commonly by way of lymphatic extension and invasion of the capsule than by vascular invasion and that harmless looking papillary cystadenomas of the thyroid tissue as well as the more complex mixed papillary tumors, may cause death (Figs. 4 to 19). Figures 30 to 35 illustrate the fact that not only tumors of mixed papillary and nonpapillary elements but also simple papillary tumors of thyroid tissue may give rise to distant metastatic lesions.

The following report of 2 cases will serve to emphasize that a patient with lateral aberrant thyroid tumor together with grave metastatic extension such as to the lungs may live a long time and that a low grade tumor that has been present for years may bring about a fatal termination.

CASE 7 (Fig. 34). A girl, aged 9 years, was brought to the clinic because of rapidly growing multiple tumors of anovular dimension under the left sternocleidomastoid muscle enlargement of the left lobe of the thyroid gland had been noted for months. The child, as horse and examination revealed that the left carotid, as fixed. Diagnosis as made of cervical malignant disease. Biopsy of left cervical node disclosed carcinoma, grade 2, in an adenoma.

metastatic from the thyroid. The tumor was solid, composed chiefly of nonpapillary elements with a few papillary elements. Mitotic figures were rare, vascular invasion had not occurred and lymphoid tissue was not present. The condition of the thyroid was inoperable. Treatment by heavy radiation was given.

A year and a half later pulmonary metastatic lesions developed, for which roentgen therapy was applied at repeated intervals. Eleven years after her first examination at the clinic the patient died of carcinoma of the thyroid with metastatic extension to the lungs.

CASE 8. A man, aged 28 years, had had multiple tumors in the right and the left posterior triangles for 14 years. The growths had increased in size in the 3 months previous to his admission to the clinic. For two years the left lobe of the thyroid had been greatly enlarged, the right lobe less so. Examination revealed that the left vocal cord was fixed. The clinical diagnosis was of lymphoblastoma. Biopsy of a left cervical tumor revealed papillary adenocarcinoma, which was diagnosed as metastatic from carcinoma primary in the thyroid. The tumor was cystic, contained occasional mitotic figures, capsular invasion had occurred, lymphoid tissue was not present. The condition of the thyroid was inoperable. The patient was treated by intensive radiation.

As the result of repeated application of radiation, the cervical tumors remained stationary for 14 years, when the patient died from carcinoma of the thyroid.

In our opinion, the most likely explanation of the presence of benign thyroid tumors (Figs 1, 2, and 3) in the side of the neck, separate from the thyroid, is the pinching off of adenomatous masses from a large nodular goiter by surrounding structures, especially muscles, these masses then drift laterally or upward (24, 28). Analogous cases have been reported in which large adenomas were found in the thorax completely separated from the mother tumor.

CONCLUSIONS

1. So called lateral aberrant thyroid tumors are nearly always metastatic extensions to the deep cervical lymph nodes from a primary carcinoma in the homolateral lobe of the thyroid gland.

2. Seventy-four per cent of these tumors are papillary adenocarcinomas and spread by lymphatic extension.

3. Sixty per cent of "lateral aberrant thyroid tumors" are associated with thyroid tumors of identical structure which always are situated on the same side.

4. The "aberrant" tumors should be treated by radical block dissection of the neck and removal of the corresponding thyroid lobe, whether or not a tumor can be felt or seen in that lobe at the operating table.

5. Complete removal of all nodes and thyroid tissue known to be involved is essential if recurrence is to be prevented. Treatment by radiation is of questionable benefit unless surgical removal of the diseased tissue has been complete.

6. Following complete surgical removal the prognosis is good in cases of papillary and low grade nonpapillary carcinomas because the rate of growth of these lesions is very slow and these tumors do not commonly invade surrounding structures, in the inoperable or neglected cases, they may have little effect on the patient's general health for years but they eventually may cause death.

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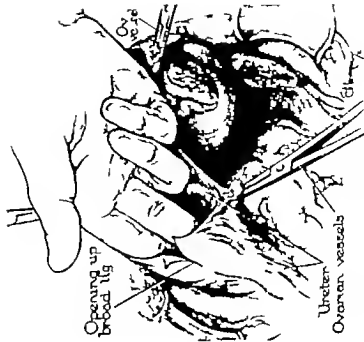
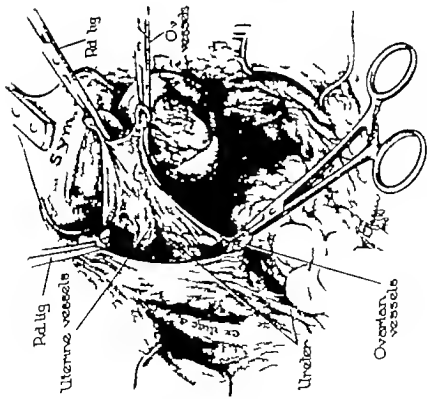


Fig. 2.

The Removal of the Right and Left Nephros i. C over f the Bod of the I. h. as—II. II. Feb. 24

THE REMOVAL OF THE REGIONAL LYMPH NODES IN CANCER OF THE BODY OF THE UTERUS

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IT is a recognized surgical fact that any operation for cancer is incomplete unless the regional lymph nodes are removed. The lymph vessels that drain the body of the uterus are found in the suspensory ligament of the ovary, along the uterine vessels, and the round

ligament. The nodes lie along the uterine, external, and common iliac vessels. An inconstant node is found at the internal inguinal ring. An operative procedure embodying these principles is presented.

The technique of the operation The patient is placed in the lithotomy position, and the vagina is thoroughly cleansed and disinfected. A catheter is passed. The external os is oversewn. This pre-

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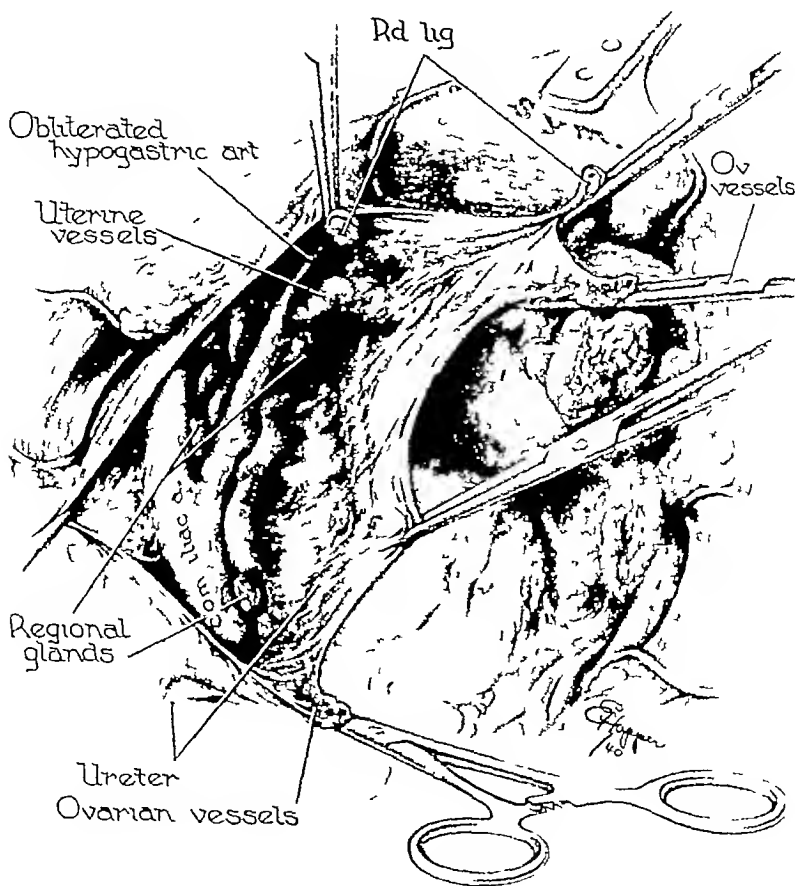


Fig 3

vents soiling of the field with malignant cells when the uterus is being removed.

The patient is now changed to the Trendelenburg position and the abdomen is opened. The round ligament is identified at the internal inguinal ring, clamped, and divided. The ovario-pelvic ligament containing the ovarian vessels is clamped and divided. The ureter is very superficial at this point, and should be identified before the forcep is applied. The uterus is firmly drawn to the opposite side by traction on the two forceps (Fig. 1). The other forceps are separated and the broad ligament is opened up widely. This

is carried out by inserting two fingers between the leaves of the broad ligament and incising the anterior fold of peritoneum, outside and parallel to the ovarian vessels (Fig. 2). The cellular tissue is brushed aside by blunt and sharp dissection. The regional nodes lying along the uterine, external, and common iliac vessels are removed (Fig. 3). A similar procedure is done on the opposite side.

Pan hysterectomy is now performed. Since the ureter is discernible at all times it is never injured. This preliminary anatomical dissection also makes the hysterectomy easier, safer, and is much more radical.

THE DIAGNOSIS AND MANAGEMENT OF INCARCERATED AND STRANGULATED FEMORAL HERNIA

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THERE has been a recent revival of interest in the treatment of incarcerated and strangulated femoral hernia. The hope of lowering the prevailing very high mortality rate seems to have furnished the incentive. The more favorable outlook, which has resulted from advances in the management of most forms of intestinal obstruction, has not been shared by those patients in whom the obstruction has been due to incarceration or strangulation of a femoral hernia. In a recent article, Dunphy calls attention to the seriousness of this condition and lists three factors which he believes have contributed to the high mortality rate: (1) delay in treatment, (2) the advanced age of the patients, (3) improper surgical management.

DIAGNOSIS

Delay in treatment is often due to error in diagnosis, and this is frequently the result of failure to examine for a mass in the femoral region in the presence of preobstructive gastrointestinal symptoms, or failure to appreciate the significance of a femoral mass when it is noted.

Dunphy points out that the diagnosis of a strangulated femoral hernia usually can be established clinically if it is given due consideration. Whenever a patient, especially a woman past middle life, complains of unexplained gastrointestinal symptoms, obstipation, and particularly abdominal pain and vomiting, the possibility of a strangulated femoral hernia should be considered. A proper appreciation of these remarks will prove to be the first step toward a reduction of the prevailing high mortality rate.

One of the most common causes of intestinal obstruction is incarceration of abdominal contents in a hernial sac. Examination, therefore, of the site of the hernial rings is necessary to make a diagnosis, because local pain may be so mild that it does not direct attention to the seat of the trouble. The mass is commonly small in size and for this reason, in some instances, the patient or the surgeon may fail to appreciate the relation between the abdominal symptoms and the unobtrusive mass present in the groin.

The anatomical relations of the sac in a femoral hernia are such that once the sac has appeared in the groin it is seldom replaceable into the abdomen, even by manipulation. The narrow neck of the sac and the small size of the femoral canal provide circumstances which occasionally result in strangulation of the sac alone (Figure 1, a and b). It may be difficult at times to differentiate this condition from strangulation of the contents of the sac. The relation of the sac to its contained structures is such that incarceration of the contents of the hernial sac can occur with relative ease (Fig. 1).

Acutely inflamed lymph nodes in the groin in an elderly individual may be confused with a strangulated femoral hernia (Fig. 2). This is due to the similarity of the constitutional and local disturbances in both conditions.

The differential diagnosis of a femoral hernia from an inguinal hernia can be made by noting the relation of the swelling in the groin to the pubic spine. In femoral hernia the neck of the sac is always lateral to the pubic spine, while in the inguinal hernia the sac makes its exit from the abdominal wall above or medial to the pubic spine. This difference in the site of exit from the abdomen usually can be seen on inspection while the patient is standing and bearing down to increase the intra-abdominal pressure. In the recumbent position many inguinal hernias are spontaneously reduced and thus lose their physical manifestation. The sac of a femoral hernia, however, will persist in place, even though it is freed of its contents, and it can be palpated lateral to the pubic spine. When incarceration of contents occurs, the differentiation between an inguinal and femoral hernia usually can be made by noting the relation of the mass to the pubic spine (Fig. 3). In each instance the mass may lie in the femoral or inguinal regions, but in the femoral hernia all of the mass is lateral to the pubic spine.

We have felt that the study of a series of consecutive cases of strangulated femoral hernia, with the emphasis placed on certain important findings, should yield a better insight into the problems of diagnosis and management of such conditions.

TABLE I.—INCIDENCE OF INCARCERATION AND STRANGULATION IN FEMORAL HERNIAS, COOK COUNTY HOSPITAL, 1931-40, TREATMENT

Year	Cases	Incarcerated	Reduced or not operated upon	Operated upon
1931-32	66	33	—	—
1933-34	86	90	5	37
1935-36	99	5	4	4
1937-38	88	26	5	4
1939-40*	63	35	9	26
Totals	404	5	32	3

*T April, 1940.

STUDY OF 225 CASES OF STRANGULATED OR INCARCERATED FEMORAL HERNIA

In a series of 404 patients with femoral hernia admitted to the Cook County Hospital during the past 9 years, it was found that in 225 (55.7 per cent) there was incarceration or strangulation of hernial contents at the time of admission (Table I). In 46 of these 225 patients nonoperative reduction of the contents of the hernial sac into the abdomen was possible. These patients were relieved of their symptoms. In 6 instances the hernia could not be reduced manually and the patients died before operative reduction could be attempted. Some of these deaths could be attributed directly to complications incident to the strangulation of the hernial contents, while in other patients there was no direct relationship between the cause of death and the pathological condition of the hernia. One hundred and seventy-three of the 225 cases required and received urgent surgical care. Of these 121 were females and 52 were males, distributed in age groups as listed in Table II.

NONOPERATIVE REDUCTION OF HERNIAL CONTENTS

In the 46 patients who had nonoperative manipulative reductions of their hernia, there were no failures to relieve the symptoms immediately. Many of these patients, however, returned at a later date for elective surgery.

The technique of nonoperative reduction is based on the anatomical configuration of the sac

TABLE II.—DISTRIBUTION OF OPERATIVE CASES OF INCARCERATED AND STRANGULATED FEMORAL HERNIA BY AGE GROUPS

Age	Number operated upon	Age	Number operated upon
5 years	5	1 to 20 yrs	33
1 to 20 yrs	6	20 to 30 yrs	42
20 to 30 yrs	3	30 to 40 yrs	35
30 to 40 yrs	24	40 to 50 yrs	5
40 to 50 yrs	35	50 yrs	—
Under 40 years of age—9 cases			
Over 40 years of age—54 cases			

and its relation to the surrounding structures. Pressure directly against the fundus of the hernial mass is inclined to increase the difficulty of reduction, because this maneuver tends to increase the angulation of the sac which is usually present where it turns abruptly to pass under the inguinal ligament. Gentle stroking of the mass downward and slightly inward with the hand will decrease the angulation just mentioned, and if the patient is supported in a moderate Trendelenburg position, it will facilitate the reduction of the contents of the hernial sac (Fig. 4). It is inadvisable to persist too long or to be too vigorous in one's attempts to reduce a femoral hernia. The communication between the peritoneal cavity and the sac may be too narrow to allow replacement of distended bowel, edematous omentum, or viscera. There have been many reports of the rupture of strangulated, necrotic bowel by too vigorous manipulation.

OPERATIVE MORTALITY

In the patients operated on (173) there were 40 deaths, or 23.1 per cent (Table III). There is a striking correlation between the mortality rate and the duration of symptoms. Fifteen patients were operated on within 24 hours of the onset of symptoms and only 6.6 per cent died. In 4 patients on whom the operation was performed a week after the onset of symptoms there were 9 deaths, 30 per cent (Table IV).

TABLE IV.—MORTALITY RATE IN RELATION TO DURATION OF SYMPTOM

Duration acute symptoms	No. cases	Deaths	Percentage
less than 24 hrs	5	—	0
2 hrs to 2 days	7	—	0
3 to 4 days	7	5	71.4
4 to 6 days	20	20	100
6 to 10 days	8	—	0
1 to 2 weeks	5	4	80
Total	72	40	55.6

TABLE III.—OPERATIVE MORTALITY RATE

Age	Operated	Died	Mortality rate per cent
1931-32	—	6	60
1933-34	37	8	21.6
1935-36	4	—	0
1937-38	4	—	0
1939-40	26	4	15.4

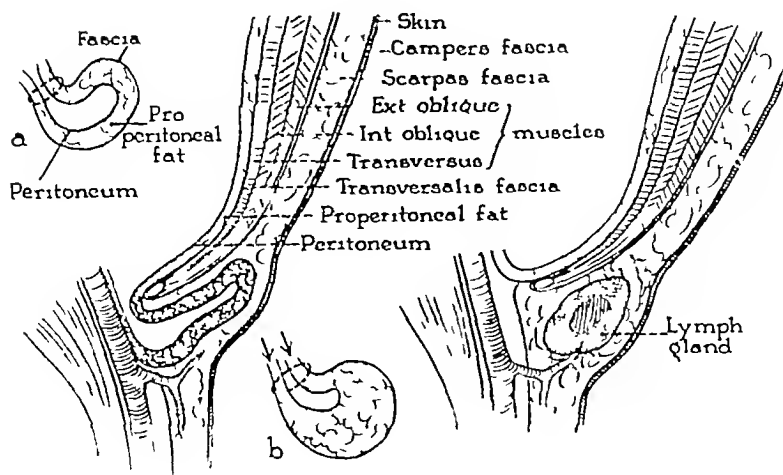


Fig 1

Fig 2

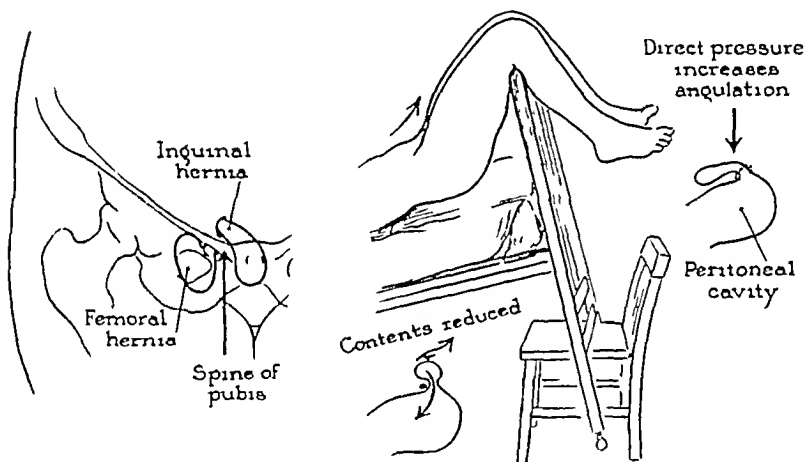


Fig 3

Fig 4

Fig 1 The layers of the abdominal wall at the site of the femoral hernia a and b Variations in the extent of the fatty layer I frequently this fat may be lobulated giving the sac an irregular contour, instead of the smooth surfaces illustrated

Fig 2 An enlarged gland in the cribriform fascia may be mistaken for an incarcerated hernia, especially when suppuration of the gland is present

Fig 3 The relationship of the neck of the femoral hernia and the inguinal hernial sac to the spine of the pubis

Fig 4 Direct pressure against the sac makes the angle at the neck more acute and reduction is then rendered less likely With the patient in the Trendelenburg position, stroking of the sac toward the knee may aid in the reduction of the contents

SURGICAL PATHOLOGY

Contents of the sac The contents of the sac in our reported cases varied as shown in Table V In 10 instances there were no contents in the sac In these the sac itself was either incarcerated in the femoral canal or strangulated, and the condition of the sac alone was responsible for the pa-

tient's complaint These cases are the basis of a separate report which has recently been published (2)

When intestines were incarcerated in the hernial sac, an elevation of temperature was usually present (Table VI) A rapid pulse rate was an almost constant accompaniment

resulting changes in the blood chemistry and body tissues which ensue following the creation of an intestinal fistula. The avoidance of the fistula if possible, is most desirable, and one should make every effort to restore the continuity of the intestinal tract.

SUMMARY

In a consecutive series of 404 patients with femoral hernia admitted to the Cook County Hospital from June 1931 to April, 1940 225 were incarcerated or strangulated on admission. Attempts at nonoperative reduction of the contents of the hernial sacs were successful in only 46 instances. Six patients died before operative reduction could be done. One hundred and seventy three patients received surgical treatment. Sixty per cent of the patients with gangrenous bowel died (20 of 33 cases). In the absence of gangrene of the intestines the mortality rate was only 14 per cent (20 of 140 cases).

CONCLUSIONS

1. The diagnosis of incarcerated and strangulated femoral hernia must be made early if treatment is to afford a reduction in the prevailing high mortality rate.

2. Intestinal obstruction, partial or complete due to a femoral hernia in elderly individuals, must be suspected, sought for and treated early because gangrene of bowel jeopardizes recovery from this serious condition.

3. Restoration of intestinal continuity following bowel resection is more desirable than the establishment of an enterostomy.

4. In the operative treatment the sac should be opened and the contents inspected before the femoral canal is enlarged. This will avoid accidental reduction of the hernial contents before examination of questionably viable viscera is possible.

5. Enlargement of the femoral canal is accomplished by severing the lacunar and, if necessary the inguinal ligament adjacent to the pubic spine.

6. A minimum of suture material should be used to approximate the inguinal ligament to the pectineus fascia, and the closure of the incision should be made with interrupted sutures not too closely spaced.

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ANESTHESIA IN CASES OF POOR SURGICAL RISK

Some Suggestions for Decreasing the Risk

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WHEN a patient who is classified as presenting a poor surgical risk comes to operation today, he stands a better chance of withstanding the effects of both the anesthesia and the operation than he did a few decades ago. Advances in many fields of medicine have helped to decrease the risk of operation and anesthesia in these cases. For instance, the use of insulin for diabetes, together with other methods of treatment, has reduced greatly the incidence of complications which accompanied surgical procedures on such patients. The preoperative management of patients who have thyrotoxicosis has reduced the morbidity and mortality rate accompanying thyroidectomy. Improved operative procedures have decreased the risk in certain fields, such as the present method of transurethral prostatic resection for prostatic hypertrophy.

Advances in the field of anesthesia and its related specialties have been of prime importance in the successful preoperative, operative, and postoperative management in cases of poor surgical risk. These advances are classified broadly as follows: (1) the evolution of less toxic anesthetic agents, (2) improved methods of administration of anesthetic agents, (3) the use of a combination of agents and methods, thereby decreasing the toxicity resulting from the use of a single agent, for instance, the so called balanced anesthesia as previously described by one of us (Lundy, 25), (4) improved methods of administration of oxygen and other inhalants, (5) supportive measures during the operative and postoperative period and (6) special measures, such as the use of tracheo-bronchial aspiration after operation. Finally, the skill and versatility of the anesthetist must be considered as important contributing factors to the welfare of the patient for whom the risk of operation is great. The patient's life often depends more on the way a certain anesthetic agent is administered than on the effects of the anesthetic agent itself.

Various methods have been employed in grading the degree of risk which each patient presents.

Saklad (36), as a member of a committee of the American Society of Anesthetists, Inc. studied problems of classification of anesthetic data and suggested that the term "operative risk" be supplanted by the term "physical state." The reason for this suggested change was for the purpose of limiting many variable factors, such as the type of operative procedure, ability of the surgeon and anesthetist, and the type of anesthetic agent the patient will receive. On the basis of "physical state," 4 classes were made, with two additional classes for emergencies. In brief, the first 4 classes are as follows:

In class 1 are included cases in which organic pathological change is absent or the pathological process is localized and does not cause any systemic disturbance or abnormality, for example, any type of operation for fractures without shock or loss of blood or uncomplicated hernias.

In class 2 are included those cases in which a moderate but definite systemic disturbance, caused either by the condition that is to be treated by surgical intervention or which is caused by other existing pathological processes is present, for example, mild diabetes, mild acidosis, moderate anemia, or mild thyrotoxicosis.

In class 3 are included those cases in which severe systemic disturbance from any cause or causes is present. It is not possible to state an absolute measure of severity, as this is a matter of clinical judgment. For example, these conditions include complicated or severe diabetes, combinations of cardiac disease and respiratory disease, pulmonary tuberculosis associated with tachycardia or dyspnea, and severe accidental trauma associated with shock.

In class 4 are included those cases in which extreme systemic disorders already have become a threat to life regardless of type of treatment. For example, these disorders include cardiac decompensation, a combination of cardiovascular-renal disease with marked renal impairment and of an operation on a patient already in poor condition to arrest hemorrhage after much loss of blood.

From the Section on Anesthesia, Mayo Clinic.
Read before the meeting of the Range Medical Society, Hibbing,
Minnesota, July 22, 1941.

One of us (Lundy) suggested a brief classification of operative risk as follows: grade 1 patients in such good physical condition that they will probably tolerate any anesthetic agent well; grade 2 cases of so-called average risk, in which the risk of the operation is greater than the risk of the anesthetic; grade 3, patients for whom the anesthetic agent must be selected with care since owing to pathological conditions, the risk of the anesthetic is as great or greater than the risk of the operation; and grade 4, patients who are in such serious physical condition that the use of any anesthetic agent is dangerous. For such patients, local infiltration may be used to control the pain but only half the concentration and half the usual amount of solution should be employed.

The risk of operation in a certain case can be evaluated intelligently only after all findings from physical and laboratory examinations are available. In certain cases, the effects of pathological lesions are so well marked that the risk is obviously poor. In others, there may be a number of obscure and less marked pathological changes which do not become apparent until the results of a complete examination have been obtained.

All anesthetic agents may be toxic to human tissue, but certain organs and tissues may suffer more acutely than others. The liver and kidneys usually are affected owing to their functions of detoxication and excretion (32). Certain anesthetic agents produce specific damage to certain organs, such as damage to the tissue of the liver by chloroform. When pre-existing damage to such an organ by some pathological process is present, the toxic effect of the anesthetic agent becomes more marked and results in greater inhibition of function. Therefore, in choosing the anesthetic agent for a patient who presents a poor surgical risk, the main factor to consider is to what extent the agent or agents will affect physiological processes already impaired. It is difficult and impractical to attempt to lay down general rules as to the choice of anesthetic agent for these patients, as each presents an individual anesthetic problem.

(3) The method of choice is one which will produce the least deleterious effects in the light of the existing pathological processes and which, at the same time, will be adequate for the anticipated operation. By the choice of the proper anesthetic agent, skillfully administered and preceded by careful preoperative preparation of the patient and accompanied by suitable supportive measures, it is possible to improve the status of his risk from one of doubtful outcome to one which offers him more than a reasonable chance of satisfactory convalescence and recovery (1, 37).

GENERAL FACTORS CONTRIBUTING TO THE PATIENT'S RISK

A few basic facts which can be ascertained from the physical and laboratory examinations usually will be all that are required in order to form a fair approximation of the risk of anesthesia and operation in a particular case. Important among these are the estimation of hemoglobin, the level of blood pressure, findings on urinalysis, degree of cardiac and renal sufficiency and the general appearance of the patient in regard to nutrition, debility and loss of weight. Although a more detailed examination may uncover further evidence of physiological abnormalities, such information may not be essential to the choice of the safest anesthetic agent. If these salient features are weighed and estimated carefully, it is not essential that facilities for a thorough laboratory examination be available. Some of the more ordinary factors to consider follow.

Age. Anesthesia and operation are not tolerated as well by patients at the extremes of life. The respiratory system of infants and young children is depressed easily by anesthetic agents. Debility and cardiovascular-renal disease may be complicating factors in the cases of aged persons. Miller observed that the mortality rate of surgical patients more than 50 years of age was eight times as great as that for patients less than 50. The need for supportive treatment should be anticipated for aged patients (18). Elderly patients fare better after operation if they are gotten up out of bed at the earliest possible time.

Habits. The mode of life of a patient has a bearing on the risk. Those who use tobacco excessively and have accompanying bronchitis are prone to respiratory complications after anesthesia and operation. Chronic alcoholics usually fare poorly under anesthesia and seem more susceptible to complications during the postoperative period. The same applies to drug addicts, since there are often accompanying nutritional and nervous disturbances.

Nervous system. Patients who are "high strung" usually are more difficult to anesthetize than those of more stolid type. Those who come to the operating room worried, frightened, and with the mental attitude that death is imminent or that they cannot survive the operation do not present a good risk and often have a stormy convalescence. Adequate preliminary medication and assurance are important therapeutic measures in these cases.

Toxic states. Toxemia, whether attributable to systemic or malignant disease, infections, or other causes, increases the gravity of the risk in direct proportion to the degree of toxemia present.

Debility Patients who are frail, debilitated, underweight, and poorly nourished lack the reserve of robust patients to withstand the toxicity of anesthesia and the shock associated with the operation. The risk of operation on markedly debilitated patients is always high. The vital functions of these patients are depressed by even small doses of anesthetic agents and great caution must be observed to prevent overdosage. Prolonged vomiting is serious, since it leads to nutritional disturbances, decrease of glycogen in the liver, and to the more serious conditions of acidosis and ketosis. The other extreme, also serious, is alkalosis, which can be produced, among other conditions, by intestinal obstruction.

Obesity Obese patients need not necessarily present a poor surgical risk, but by and large a patient who is grossly overweight does not have as good a chance of withstanding anesthesia and operation as one whose weight is nearer a normal figure. In the cases of obese patients, the operative manipulations often are more difficult and fatty infiltration of the cardiac muscle may be present, thereby lowering cardiac reserve and more or less inhibiting respiratory exchange.

HEPATIC FUNCTION

The liver and the state of its function have an important bearing on the anesthesia and its effect on the patient (31). One of the principal functions of the liver is its power of detoxification, including detoxification of certain anesthetic agents (3). In addition, the functions of the liver are inhibited and liver tissue is damaged by the action of certain anesthetic agents in the body. Bourne stated that with the exception of cyclopropane, all anesthetic agents may cause some impairment of hepatic function. The normally functioning liver, however, handles the strain imposed on it by anesthesia and operation well, provided its store of glycogen is adequate and anoxia is prevented. If its function has been impaired by toxemia and if nutritional disturbances have depleted its supply of glycogen, it then not only performs its normal functions poorly, but its vulnerability to further damage from the anesthetic agent is increased. The malfunctioning liver invariably has a low content of glycogen which always increases the risk from the anesthesia and operation. The most toxic anesthetic agent to hepatic tissue is chloroform, manifested by toxic changes in the lobules of the liver, degeneration and necrosis, leading to inhibition of function of varying degrees. For this reason, chloroform anesthesia has been largely abandoned. Divinyl ether anesthesia also may damage the liver, particularly if the

state of anesthesia is prolonged, but not to the extent or with the frequency of that produced by chloroform. Ether anesthesia impairs the function of a normal liver slightly, causing diminution of its content of glycogen, hyperglycemia, and decrease in hepatic secretion, but normal function is soon resumed during the postoperative period. Cyclopropane has little, if any, deleterious effect on hepatic function, and the same is thought to be true in the case of the very short acting barbiturates.

The best means of protecting an impaired liver are diet high in carbohydrates in order to increase the content of glycogen of the liver before operation and the maintenance of adequate oxygenation during the anesthesia and after operation. In cases of obstructive jaundice, in which the prothrombin time is increased and postoperative hemorrhage is feared, treatment with vitamin K before operation is indicated (38). Allen and Livingstone stated that the early postoperative fall in prothrombin in cases of jaundice and biliary fistula seems to be caused primarily by the inadequate administration of vitamin K before the operation, rather than from anesthesia, operative trauma, or hemorrhage. Blood transfusions are also of value. Adequate oxygenation during anesthesia is of the utmost importance in protecting the liver against the toxic effects of anesthetic agents.

RENAL FUNCTION

Although the kidneys are affected directly by certain anesthetic agents, their function also is impaired indirectly as a result of the effect of the anesthesia and operation. Chloroform may produce direct damage to the renal epithelium. Ether anesthesia causes a marked decrease in urinary output, ending in almost complete suppression after an hour or more of anesthesia. Normal function is resumed in the first 24 hours after operation. Cyclopropane anesthesia also suppresses urinary output during anesthesia; this is followed by a compensatory increase in excretion after operation. Tribromethanol anesthesia also causes urinary suppression and Veal, Phillips, and Brooks have shown in rabbits that when even mild degrees of nephritis are present, the margin of safety with this type of anesthesia is small (41). If, at the time of operation renal damage has occurred, anesthetic agents which are toxic to renal tissue and tend to inhibit renal function will produce more drastic disturbances in these organs than if they were normal. Thus, renal insufficiency markedly increases the gravity of the patient's risk.

Indirect effects of the anesthesia and operation also have an important bearing on renal function. These effects, according to Beecher, depend on several things. A marked fall in blood pressure during operation can diminish and arrest urinary secretion. Asphyxia may cause constriction of the renal vessels, leading to diminished blood flow through the kidneys and decreased formation of the urine. Owing to the resultant local anoxia the glomerular epithelium is damaged and permits the passage of albumin, proteins, and blood. Loss of fluids and blood during the course of the operation also contributes to postoperative anuria. In cases of advanced nephritis the risk of operation is not good, and nephritis often is accompanied by arteriosclerosis, hypertension and cardiac insufficiency which further increase the gravity of the risk (33). In such cases, careful tests for renal function should be performed and the level of blood urea and nonprotein nitrogen should be evaluated. In the preparation of such patients for operation, the values for blood urea, creatinine and nonprotein nitrogen should be reduced as far as possible by forcing fluids and intravenous therapy before operation. If these values stabilize readily to values not grossly abnormal, the patient may stand operation and anesthesia satisfactorily.

CARDIOVASCULAR SYSTEM

Cardiac insufficiency if advanced and uncompensated, forms one of the gravest complications the anesthetist has to face. However, it is agreed among cardiologists that patients who have many types of cardiovascular conditions, provided that compensation is adequate and cardiac reserve is satisfactory stand anesthesia and operation reasonably well (17). Patients who give the most concern are those who have advanced myocardial degeneration accompanied by circulatory insufficiency and marked dyspnea. Although a careful cardiovascular examination should be routine before any operation, a fair estimate of the patient's cardiac reserve may be obtained from information the patient can supply. If he does not have dyspnea or precordial pain either with or without moderate exertion, and if he is able to carry on the usual activities of daily life, it is probable that his heart will stand the strain of anesthesia and operation. The risk increases in proportion to the extent with which his activities are limited by the cardiac condition. If hypertension itself does not increase the risk markedly, provided cardiac reserve is satisfactory. From a review of the literature Woodbridge stated, "it is generally agreed that coronary occlusion, angina pectoris, congestive failure and syphilitic

aortitis carry high operative mortality and that valvular heart disease and auricular fibrillation if uncomplicated by failure, and paroxysmal auricular flutter fibrillation, or tachycardia do not add appreciably to the anesthetic or surgical risk.

RESPIRATORY SYSTEM

Disease of the lungs or of the respiratory passages obviously has an intimate bearing on the course of anesthesia, the complications that may arise and the degree of risk for the patient during and after operation. The effect is dependent on the site, nature, and extent of the lesion to what extent the lesion will interfere with the supply of oxygen and its transportation to the body tissues and the elimination of carbon dioxide. There is also the added risk of the production of other pulmonary complications after operation as a result of the anesthesia and operation or the extension of those which existed before operation. Any pathological condition which lowers vital capacity to a marked degree increases the patient's risk. Moersch stated that the closer the vital capacity approximated tidal air the graver was the risk. Examples of lesions which affect vital capacity are emphysema, abscess of the lung, tuberculosis, pneumonia, pleurisy with effusion, asthma defects of the thorax, and also certain cardiac conditions, particularly mitral stenosis.

A reduction in vital capacity always calls for particular care in the maintenance of adequate ventilation during anesthesia. The most important factor for accomplishing this is a free airway. When there is any question of difficulty in maintaining an adequate supply of oxygen, an intratracheal tube should be inserted after induction of anesthesia. Klotz pointed out that obstruction of the upper or lower portions of the respiratory tract which prevents the free passage of air to the blood and tissues is always serious. He also emphasized the great importance of terminal blockage of large numbers of air sacs, which reduces vital capacity and interferes with adequate exchange of oxygen and carbon dioxide, as well as that of anesthetic gases. One of the greatest hazards of deficiency of oxygen, as demonstrated by Courville (6, 12) is its damaging effect on the cerebral nervous system, particularly on the cerebral cortex. A few minutes of severe anoxemia may produce permanent damage. Waters (44) stressed the necessity of maintaining the integrity of the patient's mechanism for transportation of oxygen, of maintaining a free airway and maintaining adequate tidal exchange, by mechanical means if necessary. For the relief of pain, he further stressed caution in the use of drugs which may

aggravate respiratory depression and predispose to postoperative pulmonary complications (43). Asthma usually does not produce an untoward surgical risk. After both ether and intravenous pentothal sodium anesthesia, periods of relief from the asthmatic attacks have been observed.

Anemia frequently accompanies pathological lesions of the respiratory system and is present often when the patient is debilitated and when the risk of operation and anesthesia is great. This condition, owing to the lowered oxygen carrying capacity of the blood, interferes with adequate transportation of oxygen to the tissues. When concentration of hemoglobin is less than 8 to 10 grams per 100 cubic centimeters of whole blood, it is wise to give a blood transfusion before operation.

When indicated, the value of suction aspiration of the tracheobronchial tree during the immediate postoperative period is assuming major importance in relation to the control and prevention of postoperative pulmonary complications, such as atelectasis, massive collapse of the lung and bronchopneumonia (18, 30). According to Hinshaw, defective pulmonary drainage appears to be the primary cause of many cases of pneumonia after operation. If permitted to exist for long, depression of respiration during anesthesia and the formation of viscid mucus may plug a bronchus and lead to lobular, lobar, or massive collapse of the lung. The use of suction bronchoscopy is one of the greatest advances in helping to lower the incidence of postoperative pulmonary complications after anesthesia.

The administration of oxygen, whether by tent, nasal catheter, or special masks, such as the B. L. B. (Boothby, Lovelace and Bulbulian) oxygen mask, has become of routine importance in the postoperative management of surgical patients (8, 42). The administration of 100 per cent oxygen after operation has been useful in the relief of gaseous distention. Helium with mixtures of oxygen may be respired with less effort than oxygen or oxygen and air. Treatment with oxygen and helium has been beneficial after operation for patients who have asthma and mechanical obstruction to respiration as a result of infections, tumors, foreign bodies, or laryngeal edema.

DIABETES

Generally speaking, modern methods of diabetic therapy and anesthesia have lifted the diabetic patient out of the group of patients who present a poor risk. Unless these patients have other pathological conditions which in themselves would lead to abnormal hazards from surgical procedures and anesthesia, their outlook is

generally favorable. Other conditions frequently do exist in cases of diabetes, among which are tendencies to coronary thrombosis and cerebrovascular accidents. Many clinicians are of the opinion that the diabetic patient under satisfactory control can even withstand the disturbance of such agents as ether without untoward reactions. This seems to be true, but with the anesthetic agents available we are of the opinion that we are justified in using those which interfere least with carbohydrate metabolism. Ether not only elevates the level of blood sugar but tends to produce acidosis as a result of postoperative vomiting and restriction of food. Nitrous oxide, ethylene, and cyclopropane are suitable since they only slightly affect carbohydrate metabolism. Anoxemia may result in acidosis and thus, cyclopropane is preferable to nitrous oxide or ethylene, unless these agents will produce adequate anesthesia without deficiency of oxygen. Neff and Stiles found that Bourne's buffer phosphate solution reduced the incidence of postanesthetic nausea and vomiting with cyclopropane anesthesia. Spinal and regional anesthesia also are satisfactory for diabetic patients. Pentothal sodium intravenously administered and used alone or in combination with local or regional anesthesia also is advocated. If it is necessary to operate on a patient who has uncontrolled diabetes, every effort should be made to control the diabetes before the operation is performed unless the operation is urgent. When stabilization has occurred, any of the suggested methods of anesthesia which are adequate for the operation may be employed and if ether is necessary, it may be used in minimal amounts.

AGENTS AND METHODS

It would be impractical to attempt to establish criteria for the types of patients who present poor surgical risks, but brief mention may be made of the potentialities of certain anesthetic agents. A discussion of chloroform and ethyl chloride is purposely omitted because of their toxicity. Divinyl ether and tribromethanol have a place in anesthesia, but the former is somewhat toxic to the liver, particularly for prolonged administration, and the latter produces toxic effect on both the liver and kidneys and is considered safe only when used as a basal anesthetic agent.

Nitrous oxide. On the basis of its low toxicity, nitrous oxide and oxygen is safe, but the toxic effect of the anoxemia which may accompany the anesthesia definitely is deleterious. If the nature of the operation will permit adequate oxygenation, the method is commendable in cases in which

risk is poor. Local or regional anesthesia used with nitrous oxide and oxygen permits larger interventions and is relatively safe for these patients.

Ethylene. Like nitrous oxide the toxicity of ethylene is low and better oxygenation may be obtained than with nitrous oxide. Its uses parallel those of nitrous oxide.

Ether. Valuable as ether is in anesthetic practice its use should be avoided as much as possible in cases of poor surgical risk, owing to its irritating action on the respiratory tract which predisposes to postoperative pulmonary complications, and the vomiting, atelectasis, and hepatic dysfunction it causes.

Cyclopropane. The value of cyclopropane in many types of cases of poor surgical risk is incontrovertible on the basis of its low toxic effect on the liver and kidneys, its anesthetic potency with high concentrations of oxygen and absence of irritation to the respiratory system (43). Its use is particularly indicated in thoracic surgery (35).

Cyclopropane has certain disadvantages, however. It is a very potent gas and in high concentrations is thought to be toxic to cardiac muscle. Cardiac arrhythmias have been observed during the course of cyclopropane anesthesia, but ventricular fibrillation and complete heart block are among the few that are of great significance. If local or regional anesthesia is withheld used with cyclopropane epinephrine is increased from the local anesthetic solution since it increases the tendency to ventricular fibrillation (4, 10). Goedel suggested the combination of cyclopropane anesthesia with subarachnoid, peridural or local block to increase abdominal relaxation in certain cases. Another hazard of cyclopropane is anesthesia which cannot be overlooked is its explosiveness in anesthetic concentrations. It should never be used in the presence of any open or other electrical apparatus. Steps are now being taken to decrease the hazard of electrostatic sparks, among which is intercoupling of the anesthetic gas machine, patient and operating table (20). When cyclopropane is used with all proper precautions, its advantages in certain cases of unfavorable risk far outweigh its hazards.

Intratracheal anesthesia. Respiratory obstruction and resultant anoxemia should never be allowed to persist when such difficulties may be promptly controlled by passage of an intratracheal tube. In cases of great risk or in those in which complications are anticipated, its routine use may be advisable. The effortless breathing that results, the ease and control of anesthetic administration and oxygenation and the facility

of aspirating mucus through the tube, all favor better control. The intratracheal tube has another important use in addition to its use in anesthesia, that is, its value in resuscitation. Prompt resuscitative measures during operations in the presence of poor risk are required frequently. The effectiveness of treatment with oxygen and artificial respiration depends on the patency of the airway. The intratracheal tube assures a patent airway. Reid and Brace drew attention to the danger of altered cardiac and respiratory action and circulatory derangement as a result of irritation of the respiratory tract, particularly when anesthesia is light. This occurs as a result of reflex action in the autonomic nervous system by introduction of intratracheal tubes or other mechanical airways.

Local and regional anesthesia. Since procaine is the least toxic of local anesthetic agents, its use is preferred in the cases in which the risk of operation is great. Infiltration and block anesthesia, either alone or supplemented, continues to be one of the safest methods for such patients (26). In cases in which cardiac disease or hypertension is present, epinephrine is contraindicated in the anesthetic solution. Hypersensitivity to local anesthetic agents in certain cases must be borne in mind, as well as the inadvertent injection of the solution into a blood vessel.

A few regional methods may be mentioned. Cervical block, skillfully performed, produces adequate and safe anesthesia for most operations about the neck. For operative procedures on the upper portion of the abdomen, abdominal wall block, bilateral intercostal nerve block of the seventh to eleventh intercostal nerves, inclusive and splanchnic block are valuable procedures. Splanchnic block, supplemented by one of the others, in addition to either abdominal or intercostal block often is used for operations on the upper portion of the patient is unfavorable. Peridural block also may be used with relative safety. For operations on the nose, lower portion of the rectum, perineum and prostate gland, sacral block carries a relatively wide margin of safety. Individual nerve block and simple infiltration frequently are adequate procedures for small interventions.

Spinal anesthesia. Spinal anesthesia, although preferred in certain cases of poor operative risk, often is contraindicated in others. Here again, procaine is the agent of choice, but if the risk of operation for the patient is fair the use of metoprocaine may be considered because of the longer duration of effect.

Regardless of other factors, spinal anesthesia is contraindicated when the value for hemoglobin is less than 50 per cent (Dare), or persistent hypotension, disease of the central nervous system, or marked debility exists. Spinal anesthesia is the preferred method for many acute abdominal conditions and for operations in the presence of intestinal obstruction. Spinal anesthesia is safer for operations on the lower portion of the abdomen than on the upper. In considering spinal anesthesia for a patient of doubtful risk, it must be remembered that varying degrees of circulatory and respiratory deficiency are produced through paralysis of the sympathetic and intercostal nerves. These conditions increase in severity with the height of the spinal anesthesia, and this circulatory and respiratory deficiency leads to deficiency of oxygen and varying degrees of anoxemia, the dangers of which have been pointed out.

The method of continuous spinal anesthesia as advocated by Lemmon (22, 23) has certain advantages for prolonged operations in which spinal anesthesia appears to be the method of choice. Its use may be advantageous for spinal anesthesia for certain patients whose condition is unfavorable and for whom it is not desirable to give a dose of the spinal anesthetic agent sufficient for the whole operation. By using the continuous method, a minimal dose is administered and if the patient is reacting favorably to the effects of the spinal anesthetic, subsequent doses may be added as required. In this way it may be possible to prevent circulatory and respiratory insufficiency, which often occurs after a single large dose of a spinal anesthetic agent has been given.

Intravenous anesthesia. Pentothal sodium is the anesthetic agent of choice in intravenous anesthesia. Evipal soluble (sodium salt of n-methyl-C-C-cyclo hexamyl-methyl barbituric acid) although less potent, also is short acting and satisfactory. In cases in which intensive treatment with sulfanilamide has been given up to the time of operation, evipal soluble is preferred since it does not contain sulfur. Adriani (2) demonstrated that evidences of increased toxicity occur when pentothal sodium is administered to animals that have been receiving sulfanilamide. Lorhan and his associates concluded from their experiments that no cumulative toxic action on the liver or kidneys occurred from the administration of sulfanilamide and evipal soluble. It is generally felt that the concurrent use of these agents should be with caution, if at all.

Ordinary anesthetic doses of pentothal sodium have relatively little effect on the liver and kidneys, but when the drug is administered too rap-

idly or in too large doses respiratory function is depressed acutely. A 2.5 per cent concentration is preferred. The normal heart and the heart in which reserve is within normal limits tolerate the effects of pentothal sodium well. Advanced myocardial degeneration associated with dyspnea is a definite contraindication to its use. Most patients, even when debilitated and intoxicated, tolerate the effects of intravenous anesthesia satisfactorily, provided anoxemia is prevented. The risk to the patient is increased when, in order to produce satisfactory relaxation for certain operations, marked respiratory depression and anoxemia are allowed to persist.

The recent trend of opinion is pointing more and more to the increased usefulness and safety of intravenous anesthesia combined with various other methods.

Comment. If it is possible to generalize concerning anesthesia in cases of grave surgical risk, it may be said that combinations of regional anesthesia and cyclopropane and oxygen anesthesia, or regional anesthesia, intravenous anesthesia and nitrous oxide and oxygen anesthesia possess the widest margin of safety. The latter combination obviates the hazard of explosion or fire. Abdominal wall and intercostal block, when supplemented by intravenous anesthesia and the continuous administration of oxygen or 50 per cent nitrous oxide and 50 per cent oxygen by inhalation, is one of the safest methods for anesthetizing patients of doubtful risk. Light pentothal sodium anesthesia forms a satisfactory supplement to spinal anesthesia when indicated and aids in the control of nausea and mental trauma. Small doses, slowly administered, are indicated, since the circulatory and respiratory functions already are depressed by the spinal anesthesia.

RISK AND THE OPERATIVE PROCEDURE

Certain operations carry with them more than the usual degree of risk. Anticipation of the added risk of such procedures to that already existing is necessary from the standpoint of intelligent supportive therapy during the operation. Intracranial interventions usually are serious. It is important that the method of anesthesia does not elevate intracranial pressure. Open drop ether administered by means of an intratracheal tube is satisfactory for many intracranial operations, since an obstructed airway tends to elevate intracranial pressure.

Operations on the thyroid gland do not carry the risk they did in the past, owing to the preoperative management of the patient. Crile (14) stated that the only two absolute contraindica-

tions to operation on the thyroid gland are persistent delirium and persistent vomiting. Local infiltration in addition to gas and oxygen anesthesia usually is satisfactory. In cases in which the gland is exceptionally large or is substernal, the tracheal collapse because of prolonged pressure on the trachea is a serious potential complication. In such cases, intratracheal anesthesia is the safest method, or at least facilities for prompt intratracheal intubation should be available. Patients who do not respond favorably to preoperative medical treatment present more serious risks than those whose basal metabolic rate and pulse rate do drop satisfactorily after medical treatment. When the basal metabolic rate and pulse rate continue to remain above normal levels despite treatment, many surgeons prefer to perform thyroidectomy in two stages.

Most intrathoracic operations, such as lobectomy, pneumonectomy and open drainage for emphysema, carry unusual risk. All open operations on the thorax require delicate anesthetic control, owing to disturbances of respiratory function. Cyclopropane administered by means of an intratracheal tube permits better anesthetic control than any other method. This method often is chosen for operations on the diaphragm, such as in repair of diaphragmatic hernia. Slight amounts of ether sometimes may be added to increase the degree of relaxation and exposure.

Operations on the stomach, duodenum, gall bladder, liver and spleen may present serious anesthetic problems.

Either low spinal anesthesia or intravenous anesthesia with pentothal sodium as the anesthetic agent has been the preferred method for transurethral prostatic resection or for other manipulations on the urethra or bladder (39). Many of these patients are in poor condition because of their advanced age, debility and the prolonged retention of urine which has resulted in retention of nitrogenous waste products and uremia.

SUPPORTIVE MEASURES

Modern methods of preoperative and postoperative treatment and advances in the field of surgical shock and supportive therapy have changed the condition of many patients from that which constituted a poor surgical risk to one for which the risk was fair or even good. Modern methods of intravenous therapy such as administration of sodium chloride, dextrose and so forth have been important. Collier and Maddock mentioned the importance of the kidneys in maintaining water balance. They stated that for seriously ill patients, particularly those who have

a septic condition, severe disease of the biliary tract or some renal impairment from any cause an intake of water that provides at least 1,500 cubic centimeters of urine daily is often desirable. Intravenous therapy is important in maintaining water and electrolyte balance when, because of vomiting, fluids cannot be taken by mouth. Drew and associates stated that in the presence of shock treatment, to be rational, must overcome the severe arteriolar and venular spasm, the capillary paralysis and dilatation and the great volume of circulating blood volume. Hypertonic solution of sodium chloride is used successfully in relieving these effects. The use and value of chemotherapy, particularly with the sulfonamide compounds, for infective conditions, is well known.

High in the scale of importance is the treatment of shock during and after surgical operations (40). Shock occurs during operation as a result of several factors, for instance, the anesthesia, operative manipulation and trauma, dehydration, hemorrhage, fear, exhaustion, and anoxemia. Shock, as Moon has pointed out, may become a vicious cycle, associated with low blood pressure, low volume of circulating blood, and hemoconcentration. This circulatory deficiency is associated intimately with oxygen want in the tissues and with atony of the capillaries. Shock, if allowed to persist without treatment tends to become irreversible. Varying degrees of shock occur during any operative procedure, depending on the operative condition of the patient, the anesthetic, and the type and duration of the operation. It is obvious that debilitated, anemic, toxic, and functionally abnormal patients will succumb to shock both more easily and to a more profound degree than will more normal patients. Therefore, the anticipation of the need of treatment for shock is particularly important in a case in which the risk of operation is poor.

If shock is to be treated effectively it must be treated promptly. Better still, if it is known that the patient is in poor condition, the shock should be treated before it actually occurs. This is accomplished by various measures, depending on the urgency. A fall in blood pressure during the operation need not be serious if it is not persistent and if it is not associated with marked loss of fluid or blood. Vasopressor agents, such as epinephrine or neosynephrin hydrochloride, may be injected intramuscularly or intravenously in order to elevate the blood pressure. If the fall in blood pressure occurs in the presence of marked loss of fluid (profuse sweating) or is obviously attributable to hemorrhage, vasopressor agents give only transient relief and a false sense of security.

manent respiratory arrest was established for each animal by repeated experiments. For this purpose the initial dose employed was below the average of the series. It was then increased or decreased as required until we had determined the amount of the drug which produced an apparently permanent respiratory arrest in not less than 2 of 3 consecutive experiments and which, when reduced by 10 per cent produced arrest in not more than 1 of 3 consecutive experiments. When the respiratory paralysis had lasted 10 to 15 seconds the mask was removed and the animal was resuscitated by artificial respiration and the administration of oxygen. An essential feature of this technique is that the dose required for each animal is repeatedly confirmed—a procedure which helps to eliminate technical errors. After the minimal dose for respiratory arrest, as here defined, had been determined for each individual dog, a second series of 3 anesthetics was administered, each consisting of this predetermined dose. As soon as the animal had passed into deep surgical anesthesia but before the appearance of respiratory arrest, 0.05 cubic centimeters per kilogram of a 10 per cent solution of metrazol was injected intravenously—a dose of metrazol equivalent for the average adult human to 3.5 cubic centimeters of the commercial 10 per cent solution. In the event of respiratory arrest the animal was resuscitated by the same method used for the controls. There was no indication that tolerance to the anesthetics developed in the course of these experiments (5).

EVALUATION OF AN ANALEPTIC

The first step in the evaluation of an analeptic should be an accurate assay of the quantitative toxicity of the depressant. With this information as a basis it is possible to balance the antidotal action of the analeptic against a standardized depth of depression. Unless the experiments are carried out in this orderly manner the resulting data become so haphazard that the relative efficiency of the various analeptics cannot be ascertained. This is the confused situation now obtaining with respect to the relative value of the numerous drugs recommended for use in emergencies developing under inhalation anesthesia. Consequently, in this attempt to study the analeptics, our first concern has been with the development of an accurate method for the determination of the quantitative toxicity of ether, divinyl ether, and chloroform.

The best evidence for the reliability of a method of bio assay is the ability of the user to obtain consistent median doses for the production of a

TABLE I—CORRESPONDENCE OF MEDIAN MINIMAL DOSES FOR RESPIRATORY ARREST

Series*	Ether	Divinyl ether	Chloroform
A	1.65	0.70	0.175
B	1.75		0.185
C	1.60	0.66	0.180

*The number of dogs in each of the series was as follows: Series A—ether 35, divinyl ether 35, chloroform 35. Series B—ether 10, chloroform 19. Series C—ether 16, divinyl ether 19, chloroform 17.

standardized pharmacological effect. The data presented in Table I show that the technique we have devised has yielded consistent median doses for respiratory arrest in three successive series of animals. The doses given refer to cubic centimeters of the anesthetic per kilogram of dog.

EXPERIMENTAL RESULTS

1 *Influence of metrazol upon the minimal dose required to produce respiratory arrest.* The influence of an injection of metrazol upon the development of respiratory arrest following the administration of the individually determined minimal dose for respiratory arrest of the three anesthetics is shown in Table II. Data from a previous paper dealing with coramine (27) were incorporated in the table in order to facilitate a comparison of the antidotal efficiency of these two drugs.

It is apparent that metrazol, under the experimental conditions employed, is capable of significantly reducing the percentage of respiratory arrests from the minimal dose for respiratory arrest of ether and divinyl ether. Its antidotal value, however, should not be exaggerated because a much greater reduction in the incidence of respiratory arrest can be obtained if the dose of the anesthetic is reduced by only 10 per cent. The important implication of this fact for resuscitation is discussed in the next paragraphs. The percentage of respiratory arrests from the minimal doses for respiratory arrest of chloroform was not significantly reduced by metrazol. Evidently the respiratory effects of chloroform are more difficult to combat than those of ether and divinyl ether. In the case of all three anesthetics visible stimulation of respiration only occasionally followed injection of the drug. It is noteworthy that coramine completely failed to reduce the incidence of respiratory arrest from both ether and chloroform.

2 *The influence of metrazol upon the probability of resuscitation.* Resuscitation from respiratory arrest produced by an inhalation anesthetic is a race between the elimination of the toxic agent

STUDIES OF THE ANALEPTICS II METRAZOL

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In a previous paper (27) we have reported experiments dealing with the antagonistic action of coramine (nikethamide) against ether and chloroform. In this paper we present an analogous series of experiments designed to make a similar determination of the antidotal value of metrazol or pentamethylenetetrazol against overdoses of ether divinyl ether and chloroform.

Metrazol has the distinction of acceptance by the Council on Pharmacy and Chemistry of the American Medical Association. Although closely related to camphor in its pharmacological and therapeutic applications, metrazol has a more rapid and intense action due probably to its greater solubility in the body fluids. The voluminous literature dealing with metrazol up to 1937 is reviewed by Hildebrandt (2).

A definite antagonism has been shown to exist between metrazol and certain members of the hypnotic group, particularly the barbiturates. Thus, Tarlier and later Maloney found metrazol an efficient antagonist to sodium barbital in rats. Werner and Tatum and also Barlow have reported that metrazol is an efficient antagonist to pentobarbital in rabbits.

Several investigators including Hildebrandt (11), Helseels, and later Lendle found that metrazol increased the respiratory rate and volume in morphine depressed rabbits. An awakening action has been observed against small doses of avertin by Barlow but he found that metrazol was not life-saving in the presence of fatal doses of avertin. Schoen has reported that the depression produced by ethyl alcohol in rabbits is considerably reduced by metrazol but, according to McCrea and Taylor this antagonism is demonstrable in dogs only when the dose of alcohol is sublethal. In their experience lethal doses of alcohol are not successfully combated even by very large doses of metrazol.

Apparently the antidotal efficiency of metrazol, as in the case with coramine (17) varies with the depressant. Thus, Avmacher as well as Maloney and Tatum, found that there was little antagonism between urethane and metrazol in rabbits. Similarly Whitehead and Draper (26) obtained

no evidence of a diminution of chloralose or urethane depression in dogs and cats.

Although metrazol is widely employed by clinicians to treat emergencies developing under the inhalation anesthetics, there are few controlled experimental studies which support this use. Some experimenters have found it of no value. Thus Camp (4) found that metrazol exerted little or no action on the respiratory center of rabbits and dogs deeply depressed by ether and chloroform. Similar results are reported by Jackson. In deeply etherized dogs, Jackson found that metrazol produced tremors or convulsions with little or no stimulation of the respiration. Evipal depressed dogs, on the contrary responded to metrazol with marked specific respiratory stimulation and no tremors or convulsions.

It appears, therefore, that the use of metrazol against the barbiturates and certain of the other depressants is supported by a considerable body of experimental evidence. The experimental basis for the use of metrazol in emergencies occurring under inhalation anesthesia is less convincing.

TECHNIQUE

Measured per kilogram doses of ether divinyl ether, and chloroform were administered to healthy mongrel dogs by the same method which we employed in our coramine experiments. This method is more fully described in a previous paper (5). In brief the apparatus is a closed soda lime absorption system having a capacity of approximately 5 liters, within which the anesthetic is volatilized in a atmosphere of pure oxygen. The mask contains a rubber diaphragm through which by means of a syringe and needle the dose of the anesthetic is injected on to a wire screen for volatilization. The mask is fitted tightly to the dog's muzzle by means of a rubber face piece. Every effort was made to prevent gas leakage at this point and the entire system was checked frequently for leaks. Volatilization of the anesthetic within such an apparatus is rapidly completed, and the drug develops its maximum effects within a average period of 2 minutes. The experiments were performed at intervals of 4 days.

The minimal dose of each of the three anesthetics required to produce an apparently per-

which metrazol was injected. The conclusion seems warranted that metrazol increased the probability of resuscitation from a standardized dose of chloroform.

EVALUATION OF STUDY

The varied and complicated circumstances surrounding death under anesthesia always provide a plausible explanation for the tragedy but, in the final analysis, the same ultimate cause must be assigned—there has been a failure to resuscitate. Resuscitation, therefore, is the master key to safety in anesthesia.

It is something of a paradox that much of the greater safety of ether is due to the fact that it causes respiratory paralysis earlier in the course of the poisoning than is the case with chloroform. Ordinarily, in ether anesthesia the respiration ceases—that is to say, a further amount of the poison is rejected—while the circulation is still in comparatively good condition. Under these circumstances there is a greater probability of resuscitation than would be the case if, through postponement of respiratory failure, the subject inhaled a concentration of ether more injurious to the circulation. Thus early respiratory arrest may be regarded as an automatic safety mechanism which operates to limit the intake of an inhalation anesthetic to the minimal respiratory arresting dose. No such mechanism, of course, exists to protect the circulation from a fatal overdose of a nonvolatile anesthetic.

The period of time separating respiratory arrest from circulatory failure might be termed appropriately "the resuscitation interval" because it is only during this interval that attempts at resuscitation are likely to be successful. One of the most important factors operating to determine the probability of resuscitation, therefore, is the length of the resuscitation interval. It is possible, under certain circumstances, for the administration of a respiratory stimulant to shorten this interval by postponing respiratory arrest and in this way actually to diminish the probability of resuscitation unless the drug simultaneously increases the resistance of the circulation to the anesthetic. Some so-called analeptics are, at least potentially, injurious to the circulation. There is reason to believe that this may be the situation with respect to alpha lobeline (Camp, 3, Whitehead and Elliott) and coramine (Peters and Vischer).

Our own unpublished experience with lactic acid is a further illustration of this point. Lactic acid powerfully stimulates the respiration and is capable of delaying respiratory arrest from chloro-

form but it is also injurious to the circulation. Consequently, it acts to shorten the resuscitation interval at both ends: first by delaying respiratory arrest and second, by hastening circulatory failure. Although its administration results in some reduction in the incidence of respiratory arrest from a standardized dose of chloroform, any such advantage is more than overcome by the reduced probability of resuscitation, should respiratory arrest develop. Our experience with lactic acid and other respiratory stimulants has impressed us with the view that it is the behavior of the circulation which determines the final outcome of an attempt to resuscitate and that respiratory arrest, at least when produced by the inhalation anesthetics, should be treated with analeptics chosen for their circulatory rather than their respiratory effects.

The reasons for our position can be made clearer by a brief consideration of the physiology of resuscitation. In the great majority of instances respiratory arrest occurs before the concentration of the anesthetic becomes sufficient to cause failure of the circulation. Although, absorption of the poison does not continue after respiratory arrest there is, unfortunately, a rapid development of anoxemia. The ultimate failure of the circulation is the result of disastrous synergism between anoxemia and the anesthetic. Forced ventilation of the lungs following respiratory arrest merely replenishes the oxygen supply within the lung alveoli and removes the anesthetic from these passages. This alone will not ensure resuscitation. For success the circulatory minute volume must be large enough to provide effective transport of these gases between the lungs and the body tissues. The most efficient artificial respiration cannot save a patient whose circulation lacks the necessary vigor.

We have shown in Table II that the removal of a small amount of the anesthetic will act more effectively to restore spontaneous respiration than will the injection of a respiratory stimulant. Moreover, the highly developed mechanical methods now available for forcible ventilation of the lungs greatly reduce our dependence upon pharmacological respiratory stimulants. However the position is otherwise if the analeptic acts upon the circulation to speed the rate of transport of gases between the lungs and tissues. Such a drug should be a very useful aid to resuscitation.

In this connection it is of interest that an increased cardiac minute output after metrazol is observed in animals by Mueller, and by Gollwitzer Meier and also in humans by Grosscurth and Bensi and by Heun and Neuthard. Doses of

TABLE II—INFLUENCE OF CORAMINE AND METRAZOL UPON THE AMOUNT OF ETHER, DIVINYL ETHER, AND CHLOROFORM REQUIRED TO PRODUCE RESPIRATORY ARREST

Ether	No. of dogs used	Total administration of anesthetic doses for respiratory arrest	Percentage of administration remaining in arrest
MDRA alone	26		80
MDRA plus coramine	26	28	
MDRA plus metrazol	26	25	92
MDRA reduced by 50 per cent	26	54	92
Divinyl ether			
MDRA alone	19	43	
MDRA plus metrazol	29	52	93
MDR ¹⁰ reduced by 50 per cent	19	26	77
Chloroform			
MDRA alone	26	200	26
MDRA plus coramine	29	64	90
MDRA plus metrazol		54	
MDRA reduced by 50 per cent	26	64	

¹⁰The MDRA is the Metrazol Dose required to produce Respiratory Arrest at least of consecutive administrations

through the lungs and the development of its fatal effects upon the circulation. A drug can be properly termed anæsthetic only if its use helps to win this race. The definite test for anæsthetic action therefore should determine the influence of the drug upon the probability of resuscitation. So far as we are aware no other controlled studies of anæsthetics have been made which subject them to this critical test against otherwise fatal doses of the inhalation anæsthetics.

In the course of the experiments here reported we have carried out 542 resuscitations from respiratory arrest produced by overdoses of ether, divinyl ether, and chloroform both with and without the aid of anæsthetics. This has given us the opportunity to determine the influence of metrazol and of coramine upon the probability of resuscitation. All our resuscitations have been conducted under conditions controlled so as to make them identical with the exception of the anæsthetic and the anæsthetic employed. The data are presented in Table III.

TABLE III—INFLUENCE OF CORAMINE AND METRAZOL UPON THE PROBABILITY OF RESUSCITATION

Ether	No. of dogs used	Respiratory arrests produced	Failures to resuscitate	Percentage failures to resuscitate
Control resuscitations	26	26		
Resuscitations with coramine	26			
Resuscitations with metrazol	26	25		
Divinyl ether				
Control resuscitations	26	25	2	2
Resuscitations with metrazol	26	26		
Chloroform				
Control resuscitations	53	54	5	
Resuscitations with coramine	29		5	
Resuscitations with metrazol	27	27		

Of the 149 control attempts at resuscitation from an overdose of ether only 9 or 1.4 per cent resulted in failure. The relatively low probability of failure to resuscitate when ether is the anæsthetic makes it difficult to determine the value of a pharmacological antidote but, as will be noted, there were no failures to resuscitate following the administration of either coramine or metrazol. It is quite possible that the absence of failures to resuscitate in the ether experiments was due to the smallness of the anæsthetic series.

The probability of failure to resuscitate was somewhat greater in the divinyl ether series. In the 81 control attempts to resuscitate, 3, or 3.7 per cent, were unsuccessful but again there were no failures to resuscitate in the 30 respiratory arrests treated by an injection of metrazol. The probability of failure to resuscitate from an overdose of divinyl ether in the control experiments was not sufficiently high to warrant the conclusion that metrazol was an aid to resuscitation.

The much higher mortality resulting from an overdose of chloroform affords a better opportunity for the evaluation of an aid to resuscitation. In 154 control attempts to resuscitate 15, or 9.7 per cent, ended in failure. Following the administration of coramine there were 5, or 1 per cent, failures to resuscitate in 45 attempts. It is apparent that the addition of coramine did not increase the effectiveness of artificial respiration and oxygen. On the other hand, we experienced no failures to resuscitate in the 37 experiments in

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EXTENSION OF INDICATIONS FOR RADICAL OPERATION IN CANCER OF THE RECTUM

SIR W. ERNEST MILES made a noteworthy contribution to the surgery of cancer of the rectum when he emphasized the possibility of lateral and high lymphatic involvement in the disease and in 1907 strongly recommended the one stage abdominoperineal operation as the one which insured the greatest guarantee of complete removal of the carcinoma and its local extensions. In the Lettsomian lectures which he delivered in 1923 he traced the development of the surgical treatment of carcinoma of the rectum from the purely local operations to the much more radical one stage abdominoperineal operation and made a report of 116 such operations which he had performed. Radical operations were carried out in only 29.3 per cent of the patients coming under his care. Of his first 63 one stage resections there was a 36.2 per cent mortality rate and no patient over sixty survived. In the next

53 operations his mortality fell to 9.3 per cent, which he modestly attributed to the use of better anesthesia. Patients over sixty-five years of age, fat patients, patients with arteriosclerosis, diabetes, tuberculosis, Bright's disease, were considered unsuitable for operation. Growths attached to surrounding soft parts were not considered amenable to operation.

Since that time Miles' advocacy of the one stage abdominoperineal operation has been accepted as the operation of choice in many clinics and additional knowledge of the frequency of carcinomatous involvement of the lymphatic glands (65 per cent in removed specimens) as well as the height of their involvement has tended to confirm the soundness of that choice. Extension of the indications for operation has also increased in the last five years due to the maintenance of a relatively low operative mortality rate and increased knowledge as to what can be done surgically to carefully prepared patients. The extension of indications for resection of carcinoma of the rectum has been also furthered by the radioresistant character of cancer in this region, which leaves surgery as the outstanding chance for cure of these patients according to our present knowledge.

As Gilchrist and I have recently reviewed our last ten years' experience in the selection of patients with cancer of the rectum for radical operation, I was asked to comment on our findings in this editorial. The material studied concerned 277 patients coming to our service in the Presbyterian Hospital for operation. Five were considered inoperable. Two hundred seventy-two patients were operated upon and 179 had a radical removal

the order we have used in our experiments have been shown by Haury and Graber to dilate the peripheral vessels. A favorable action upon the circulation depressed by chloroform has been observed by several workers including Eichler and Hildebrandt, Russek and Spierchen and Leffkowitz.

There is thus some experimental support for the view that metrazol may aid resuscitation from chloroform overdose through a stimulant action upon the circulation which tends to lengthen the resuscitation interval and to increase the rate of gas transport between the lungs and tissues.

SUMMARY AND CONCLUSIONS

Metrazol increases slightly the amount of ether and divinyl ether but not of chloroform required to produce respiratory arrest in dogs. Only occasional brief stimulation of the respiration is seen when metrazol is injected in toxic anesthesia produced by these agents.

2. In 543 attempts to resuscitate from respiratory arrest produced by ether divinyl ether and chloroform were carried out by means of artificial respiration and the administration of oxygen with and without an injection of metrazol or coramine.

3. Of 149 attempts to resuscitate from ether overdose without the aid of an anesthetic 2 or 1.4 per cent, were unsuccessful. In 81 similar control resuscitations following an overdose of divinyl ether 3, or 3.7 per cent, ended in failure. The mortality from an overdose of chloroform was much higher and attempted resuscitation failed in 15 or 9.7 per cent of the 154 control experiments. There were 2 failures to resuscitate when metrazol was administered in addition to artificial respiration and oxygen in the treatment of 25, 30 and 37 respiratory arrests produced by ether divinyl ether and chloroform, respectively.

4. The low probability of failure to resuscitate without the aid of an anesthetic from an overdose of divinyl ether and especially from ether makes evaluation of a pharmacological aid to resuscitation difficult. When the very high incidence of failures to resuscitate from chloroform induced respiratory arrest in the control series is contrasted with the complete absence of failures when metrazol was administered, the conclusion

seems justified that metrazol was useful as an aid to resuscitation.

5. As previously reported coramine does not exert a favorable influence upon the probability of resuscitation from an overdose of chloroform.

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that the condition is far more common than had been realized. It is curious that during this period of awakened interest in anatomical defects in the diaphragm, there has been no corresponding revival of curiosity about its origin and structure. As a matter of fact, most English textbooks of anatomy and embryology have either made no changes in their discussions of this subject or have curtailed them so much in the latest editions that they leave much to be desired in both clarity and completeness. This state of affairs is remarkable in view of the fact that Ballou has shown, in a recent historical review, that the diaphragm has fascinated anatomists for centuries. Perhaps anatomy has become too completely divorced from surgery.

The diaphragm is something of an afterthought in the evolutionary process, being present as a complete septum only in mammals. The major part of it is assembled from three ill-assorted structures, the septum transversum (itself something of an embryological enigma), the pleuroperitoneal membranes, and the dorsal mesogastrium. These structures descend from the cephalic portion of the celomic cavity on different time schedules and finally unite to form a single complete septum between the abdominal and thoracic cavities at about the seventh or eighth week of fetal life. Obviously, any disturbance of the orderly progress of this intricate process may result in the formation of defects in the diaphragm.

The phrenic nerve develops and descends with the segment formed from the septum transversum and invades the remainder of the diaphragm after fusion of the three segments. If this invasion is arrested prematurely, the musculature of that part of the diaphragm that has not received a nerve supply probably undergoes atrophy, leaving only the peritoneum and the pleura to separate the two great body cavities in that particular location.

Soon after the diaphragm becomes a complete septum, the mid-portion of the celomic cavity is rapidly expanded by growth of the liver, and the resulting tension of the diaphragm causes it to pick up from the body wall a supplementary rim of tissue. One would therefore expect the diaphragm to be continuous with the inner layer of the abdominal cavity. Recent anatomical studies by D. D. Baker have shown that this is actually the case and that the conventional descriptions of the attachments of the diaphragm are incomplete and to some extent inaccurate. He finds that the anterior and lateral portions of the diaphragm are continuous with the transversus abdominis muscles and the posterior sheath of the rectus muscles. The attachment of these structures to the costal arch is by means of what is, in effect, a common aponeurosis. Likewise the posterior or lumbar segments of the diaphragm are continuous with the anterior layer of the lumbodorsal fascia, except for the central portion, which is attached to the bodies of the lumbar vertebrae.

While these observations are original with Baker, the idea is not new, for, according to Ballou, in 1676 Caspar Bartholin, son of Thomas, described the diaphragm and transversus abdominis muscles as a trigastric muscle, and in 1905 Sir Arthur Keith noted their developmental association.

A surgeon studying Baker's dissections is immediately struck by the fact that when the common aponeurosis of the transversus abdominis and the diaphragm is detached from the under surface of the costal arch, the diaphragm has been supplemented by a structurally similar fibromuscular membrane which increases its area by at least one-third. If there should be a very large defect in the anterior half of the diaphragm it could be closed without tension if the transversus abdominis were advanced into the thoracic cavity and

of the tumor with a hospital mortality of 7.2 per cent and a resectability rate of 65.5 per cent. Ninety-three patients were found to be unsuited for radical removal of the tumor due to extensive liver metastasis in 40, infiltration of the growth into the base of the bladder in 18 and marked infiltration of the growth into the prostate, vagina, or sacrum in 25.

Of the 179 patients from whom the tumor was removed 105 presented some doubtful factors concerning the possibility of completely removing the tumor or in making the operation more difficult than usual. These factors were in the main: age over sixty-five years, adiposity, one or two small suspicious nodules in the liver, obliterated pelvic peritonitis from previous pelvic operation or diverticulitis, attachment of the tumor to the bladder, abdominal wall, adnexa, prostate, bladder, urethra, vagina or sacrum and constitutional disease as diabetes or heart disease. Of this group of 105 patients the operative mortality rate was 9.5 per cent. In 74 favorable cases where there were no doubtful factors the operative mortality rate was 4.3 per cent. The long term survival rate can not be given at this time but in general it can be said that there are many of these patients who came in the doubtful group who have lived three to five years.

The consideration of a few of the doubtful groups may emphasize the value of extension of the indications for radical operation in cancer of the rectum.

There were 38 patients over 65 years of age given the benefit of removal of the tumor with four deaths (pneumonia or embolism). Nine of these patients were operated upon more than five years ago and five are still alive.

One of the most difficult decisions to make in favor of radical removal of the tumor is in the case where the tumor is adherent to

of the prostate was removed with the tumor in 5 patients, the rectovaginal septum in 6, the uterus and adnexa in 4, the ureter in 2 the dome and posterior half of the bladder in 1 and another loop of bowel in 1 patient with 2 deaths in all groups.

There were 16 patients who had one or two small nodules in the liver in whom it was difficult to be sure that the growths were carcinoma and in whom radical resections were done. Four of these patients died of cancer of the liver on an average of ten months after operation but four others are alive and well three to seven years after operation.

In very fat patients there is no doubt an added risk of hemorrhage, infection, evisceration and cardiovascular accidents, but in view of the extremely poor prognosis in nonoperative treatment we did not consider adiposity a contraindication for operation. Of eleven very fat patients there was one death from embolism and one evisceration which was repaired successfully.

No more details of problem groups will be considered here, and it only remains to suggest that radical operation for cancer of the rectum can be carried out in an increasing number of patients and that it offers the patient the best chance of cure provided the preoperative treatment of decompression of the bowel and restoration of the blood to normal (cells, electrolytes, vitamin content, sugar, chlorides, plasma protein) as well as safe anesthesia and a reasonable surgical technique are considered essential principles.

VANSON C. DAVIS.

ANATOMY AND SURGERY OF DIAPHRAGMATIC HERNIA

DURING the past twenty-five years there has been a rapid and progressive increase of interest in diaphragmatic hernia, and it has become apparent

THE SURGEON'S LIBRARY

REVIEWS OF NEW BOOKS

THE title of the informal, chatty little book *Wounds and Fractures* by H. Winnett Orr, may be misleading and prospective readers should be told that little space is devoted to the subject of wounds proper. Actually it is a treatise on fractures, in which stress is placed on the care of those associated with contaminated or infected wounds. As one might suspect from the name and fame of the author, wide open aseptic packing with vaseline gauze, coupled with rigid immobilization by the pin fixation plaster cast technique, is offered as the sine qua non of successful treatment in such cases. In this method Dr Orr is, of course, a pioneer, and throughout the book the reader will find photographs, x-ray productions, and case abstracts covering every possible situation in which the method may be used.

Innumerable useful variations in technique are found, most of them simple and appealing to those working with barest essentials. The subject matter, the arrangement in which it is presented, and the distinction of the author combine to make this a valuable work. Let those who oppose the method for various well grounded reasons review the literature emanating from Europe during the past four years, and they will find that the method is becoming less and less controversial, certainly as it has to do with the wounds of war.

Solely as a textbook on fractures it probably is not suitable for students. It seems too advanced and broad enough view of the subject is not given. It should, however, be included in any collection of fracture texts. The principal lesson which the author intends to portray for the general practitioner particularly, is that the compound infected fracture, even with loss of substance, does not necessarily call for amputation. J. K. STICK

THE volume *Diseases of the Thyroid Gland* representing forty years of experience, dedicated to the author's grandchildren—'fellow students in medicine'—merely half a century behind him is not intended as a treatise on disease of the thyroid gland, but as a record of studies. It makes most entertaining reading and stimulating study. Anyone who makes no belabored assertion, so permissively and denies self evident conclusions so forcefully is bound to stir up thought and this is certainly the main object of this book. The text is written in conversational style which makes the reading so

easy and rapid that before you know it you are taking something for granted which is certainly not the intention of the author. The thought provoking character of the text may best be illustrated by a quotation: "Myxedema is a clinical term signifying a myxoid edema of the subcutaneous tissues. It is presumably due to lack of thyroid secretion. This opinion is based on the fact that the condition is ameliorated by giving thyroid extract. This represents about the sum total of our knowledge and has in a measure closed our eyes to some very obvious facts. It is first of all to be realized that the term myxedema is not synonymous with deficient thyroid secretion. This belief has been one of the sacred cows in medicine and any one who made merry with the old bossie did so at his peril, but the old critter has gone to the hamburger factory for ignominious extinction. It is important to keep this in mind because we know now that there can be a deficiency or an absence of thyroid secretion without any of the clinical signs of myxedema, as total thyroidectomies have abundantly shown. Nor is myxedema the superlative degree of thyroid dysfunction or the physical expression thereof. In cases in which myxedema is associated with a waning hyperthyroid state we have a combined minus and plus state. Our sacred bossie has become a hermaphrodite. This emphasizes the paucity of our fundamental knowledge." This paragraph reproduces the mixture so characteristic of the author's work, namely, of denial of much that has been scientifically demonstrated by others with violent assertion of personal knowledge certainly not shared by many students of thyroid physiology.

The volume contains 670 pages, is fully illustrated and well indexed and will be enjoyed and valued by all interested in diseases of the thyroid.

PAUL STAMP

A COMPLICATION of the experience and an outline of the routine in the care of premature infants at the Sarah Morris Children's Hospital of the Michael Reese Hospital in Chicago are presented in *The Premature Infant* by Hess and Lundeen. The great detail and step by step description of equipment and its use in the care of the premature infant should make this a good manual for any one interested in the birth or premature nursing setup. Although elementary in some respects it should be a

made to become a part of the diaphragm. Cadaveric dissections have shown that this procedure is entirely practical although it has not as yet been employed in the living subject.

Large defects in the posterior half of the diaphragm cannot be closed by this method but the principle of employing a flat fibro-

muscular sheet that, like the diaphragm itself is continuous with the body wall, can be utilized. Using a posterior transthoracic approach we have bridged the hiatus in such a case with a flap developed from the latissimus dorsi and have found that it served the purpose admirably. JAMES D. RIVER.

surgery of the heart has been pushed too much into the background

The volume contains an admirable summary of the development of the heart, as well as its comparative anatomy. The normal anatomy is given at some length, but all too often the surgical implications of anatomical facts have been slighted or completely overlooked. Cardiac histology and physiology have been summarized. The chapter on radiological examination of the heart does not discuss angiocardiology. The treatise on electrocardiograms gives a good basic presentation of the normal types of graphs but it is deficient in consideration of abnormal forms.

While one might expect to find exhaustive descriptions and illustrations of surgical procedures in a book pertaining to this field, the volume is deficient in this regard. Of a total of 268 figures, only 9 are concerned with actual surgical technique or other therapeutic procedures, and all but one have been borrowed from the previous publications of other authors.

The reader is struck by the great lack of critical analysis of the results of therapeutic procedures, such as pericardiectomy for constrictive pericarditis, of total thyroidectomy for angina pectoris, of sympathectomy for angina pectoris, of surgical closure of the patent ductus arteriosus. Regarding alcohol injections of the sympathetic ganglia for angina pectoris, there is only a single sentence regarding postinjection alcoholic neuralgia. The impression is given that such a complication is rare. Unfortunately, this is not the true state of affairs as anyone who has had any appreciable experience with such treatments has found.

The author has covered the literature exhaustively, perhaps because of too great stress in this direction and because the author has included so little of his own personal experience in cardiac surgery the present volume lacks authority. Unfortunately, too, the book has been compiled at a time when surgical knowledge has been accumulating rapidly, hence the lag incurred by the process of publication has excluded from the volume several of the more recent advances in cardiac surgery which might be appropriately included in it.

ROBERT E. GROSS

THE form of *The 1941 Year Book of Radiology*¹ follows that established by its predecessors, offering to the medical profession a review of the important articles which have appeared in the literature during the past year. As would be expected because of the war, there has been a relative scarcity of foreign material. Approximately 28 per cent of the articles reviewed in this volume come from outside of the United States. As one scans through the pages of this volume he is impressed by the immense amount of work which is required to assemble the material. As in previous years the authors present

the material in a concise but easily readable manner. Merely paging through the book will review one's reading for the past year and will no doubt reveal a number of articles which have escaped attention, making the book invaluable for reference work.

In the field of radiological diagnosis the authors have been reluctant to choose any particular work as outstanding but mention a number of interesting and refreshing subjects. Articles of interest on the osseous system include changes in the epiphyses found in observing hyperthyroid children, "pseudo-fractures" as related to faulty nutrition and military service, injuries following metrazol therapy, solitary eosinophilic granuloma, and porotic conditions. The use of organic salts of iodine in bronchography, the results of mass surveys for tuberculosis and "virus" or "type X" pneumonia, are important contributions. In the field of gastroenterology considerable attention is being given to the small bowel. The use of the Miller-Abbott tube in intestinal obstruction, and a new dye, phenyl propionate acid, for the study of the gall bladder, are subjects of more than ordinary interest.

In the introduction to the section on radiotherapeutics, Dr. Kaplan has given a very excellent, concise, and interesting review of the progress in this field during the past year. Because of the war there has been a transition from old to new world dominance in the field of medical radiology. In some countries research centers have been entirely destroyed, while in others the chief emphasis has been placed on scientific achievements associated with military needs. Because of the destruction of hospitals and medical centers in England it has been necessary to rely more and more upon radium, particularly radon, rather than x-ray therapy. There has been continued interest in the treatment of non-malignant lesions. A number of articles have appeared on the use of supervoltage therapy as compared to the conventional 200 kilovolt type. The question of whether tuberculosis can be treated by x-ray again is receiving some attention but the answers have been either cursory or negative. The question of preoperative x-ray therapy for carcinoma of the breast is still unsettled, possibly because of the great variations in methods and technique. The value of ovarian irradiation, in breast carcinoma and metastases, has received considerable attention during the past year. Paging through this section one is impressed by the great amount of work which is being carried out, particularly in the United States.

It is hoped that in spite of the interruption of the work in foreign medical centers and the currently disordered world, it will be possible for the authors and publishers to see their way clear to continue the publication of this excellent yearly review of international literature. As the reviewer has stated in previous years, he finds this volume indispensable in his work and ventures to say that this is the feeling of the great majority of radiologists throughout the country.

FARL E. BARTII

¹THE 1941 YEAR BOOK OF RADIOLOGY. DIAGNOSIS edited by Charles A. Waters, M.D., and Whitmer B. Fifer, M.D. THERAPEUTICS edited by Ira J. Kaplan, B.Sc., M.D. Chicago: The Year Book Publishers, Inc., 1941.

therapy admittedly is of the most important subjects; premarital care are very brief. The subject of vitamins is given considerable discussion and the care and management of wet-nurses. A helpful description is given of the various diagnoses and treatment procedures, such as spinal puncture and the administration of intravenous fluids. Some of the major and minor disorders that occur in the premature infant are briefly described. This book is concluded with a rather interesting and enlightening chapter on the late mental and physical development of premature infants. L. MARTIN HANCOCK

In the Oxford War Manual the author has briefly summarized the treatment of burns. Most of the English authors in the current literature are not in agreement with the tannic acid method as advocated in the volume, and there has been much added to the local treatment of burns since this volume was published.

The early chapters on classification and clinical course of burns are excellent. The method outlined for recognizing and combating burn shock and toxemia are practical and up to date.

In the complications of burns, chapter 11 the author ignores the subject of infection but later implies that infection is a normal sequel to all serious burns. This, in the reviewer's experience, is unjustified.

The greatest part of this volume is devoted to outlining in detail each step taken in the tannic acid method of treatment. It has only briefly mentioned the method of cleansing of the raw surface. This is in marked contrast to memorandum published later E.M.S./Gen/343 circulated by the Ministry of Health for the guidance of medical officers which lays great stress on the proper method of cleansing the burned area with soap and water before the wound is treated by either open or closed methods.

The final chapter on the hospital care of burns simply outlines the various equipment needed but no mention is made of the scrupulous aseptic care which must be attained to prevent infection from occurring in these large open wounds.

With the exception of burn shock, too little of recent advances on this common war injury has been mentioned. HARVEY S. ALLEN

To correlate the clinical and pathological statistics relative to cancer of the face and mouth as found in a large clinic over a period of years is a tremendous task. In a clinic where cancer work has been carried on with an open mind as to the value of the various methods of treatment the summation of these findings should prove of immense value. Drs. Blai Moore and Byars together with other mem-

bers of their staff have presented their findings in a view of the collective impression gained from the radiologist, the surgeon, and pathologist. Their broadening the scope of the book by cementing the impressions of these combined groups rather than letting one method of treatment dominate.

The authors stress again and again that the doctor first seeing the patient is responsible for his ultimate fate. The convenience of certain methods of treatment used as a substitute for surgery does not remove the responsibilities from the shoulders of those first consulted by the patient.

The book must be read carefully to appreciate fully the authors' viewpoint, but the impressions gained are unmistakable and invaluable. Force is added to their contentions by numerous excellent photographs. A unique feature of the book is a large collection of line drawings under the heading of "Operative Technique" which show graphically various steps in operative procedures, and these are in turn directly related to some particular case in the text.

A general impression of the scope of the book may be gained from a statement by Dr. Moore in which he says that the proper management of cancer means the proper co-ordination of surgery, x-ray and radium as means of therapy. The use of any one method in all cases of cancer would be to the detriment of the patient.

This book should be of immense value to surgeons, radiologists, and dentists as well as the general practitioner not only to tell them what to do but also to tell them what not to do. CLAUDE L. STUART

An attempt is made to summarize the knowledge of diseases of the heart and great vessels of the thorax in King's *Surgery of the Heart*. Unfortunately it has been given a title which does not accurately indicate its contents. While Dr. King has been primarily interested in surgical problems, the finished book has included almost all types of the pathology which might affect the heart and vessels immediately adjacent to it. A large number of conditions have been included which do not fall within the realm of surgical diseases, nor could they conceivably be brought into this field at any future time. Indeed, the medical diseases are given more space in this book than are those which are being currently treated by the thoracic surgeon. Inasmuch as such a wide range of material has been collected here in book form, the volume would probably attain a wider range of usefulness for students and practitioners if it had been published under a more general title indicating its true scope. The author has probably intended that the cardiac surgeon should be familiar with all of the major lesions which might exist in the organ upon which he is operating, but in this attempt to set forth a broad view he has produced an imbalance so that the

THE TREATMENT OF SCURVY. By A. B. WALLACE, M.B. F.R.C. Ed.
M. B. (Edinburgh). London: H. K. Lewis, 1931. 10s.
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SURGERY

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PRIMARY TUMORS OF THE SUBMAXILLARY GLAND WITH SPECIAL REFERENCE TO MIXED TUMORS

MALCOLM B DOCKERTY, M D , and CHARLES W MAYO, M D , F A C S ,
Rochester, Minnesota

IN an analysis of the array of conflicting evidence extant on the subject of "mixed salivary gland tumors," one is almost led to the conclusion that the word "complicated" should have been used as a designation for these neoplasms. That their histogenesis is still not understood is evidenced by the fact that the "mesenchymal," the "endothelial," the "branchial," the "enclavement" and the "epithelial" theories of origin still have their protagonists. The strange clinical behavior of these tumors was well expressed by Kennon who wrote, "Salivary-gland tumours, though not of frequent occurrence, share with sebaceous cysts and ganglion a peculiar power to elicit in their possessors a morbid delight in their presence, with its attendant self-pity. This, with the luxury of an ever-sympathetic group of friends, makes them blind to the hideousness of their deformity and deaf to the warnings of the profession as to the ultimate outcome of this silent death. The knowledge of surgical failures in patient and doctor alike, has weakened the demand for treatment." Nor have pathological researches on these lesions clarified the difficulty of their interpretation. Stein and Geschickter, in a report on tumors of the parotid gland, wrote as follows:

"The benign neoplasms of this organ often show malignant tendencies in that they recur frequently after simple excision, whereas the malignant tumors often show benign features in that distant metastases rarely develop. Whether recurrence in a given case is a clinical feature of a benign process or a malignant feature of a type of carcinoma in which a tendency to widespread metastases is practically absent is not always easily decided. The composition of the majority of these new-growths as seen through the microscope is likewise difficult of interpretation."

The lack of unanimity of opinion regarding the nature of these neoplasms is adversely reflected in the results of surgical treatment. Because these mixed tumors have been regarded by many as being essentially benign, surgeons all too often have yielded to the temptation to "shell them out," so to speak, especially when the tumors appeared to be encapsulated. In the case of tumors of the parotid gland this tendency toward conservatism was further influenced by the proximity of the important facial nerve. As a consequence the carrying out of radical procedures usually was avoided until the tumors recurred—a tragedy which happened all too frequently.

In recent years, however, experience has accumulated to show the necessity for revision

THE general scope and plan of the second edition of Kracke's *Hematology* is similar to the first edition. (Reviewed in this Journal in the May 1938, issue on page 944.) The material is grouped in eight sections as follows: (1) hematologic terminology, (2) the development and morphology of blood cells, (3) leucocytosis and leucopenia, (4) the anemias, (5) the leukemias, (6) hemorrhagic diseases, (7) miscellaneous, and (8) hematologic technique. The volume has been enlarged by 60 pages in order to include many of the advances in hematology during the last few years. There are new chapters on hemoglobin and its derivatives and the porphyrin compounds, the hemolytic anemias and hemoglobinuria. The table of the more common injectable iron extracts with their potency and cost will be helpful in choosing therapy for the patient with pernicious anemia. Dr. Lloyd Craver has contributed

an excellent chapter on the treatment of leukemia in which is included the use of radioactive isotopes. Other new chapters are those on vitamin K and Hodgkin disease. Subjects of current interest also added are the operation of a blood bank, plasma transfusion, and the effect of the sulfonamides on the blood picture.

Drawings of leucocytes in several new colored plates show much greater detail and are more realistic than in the older plates.

It is felt that the section on the anemias would be improved by closer adherence to an etiologic classification. In the description of the anemias, very little reference is made to cell measurements such as corpuscular volume, corpuscular hemoglobin, and hemoglobin concentration.

The complete bibliography at the end of each chapter is a very useful feature. This unique volume should continue to be a valuable reference book to physicians confronted with hematologic problems.

HOWARD L. AIR

DIAGNOSIS OF THE BLIND - AN ATLAS OF HEMATOLOGY By Roy R. Kracke, M.D. and ed. Philadelphia, (Lippincott) 1940
944

BOOKS RECEIVED

Books received are acknowledged in this department, and such acknowledgment must be regarded as sufficient return for the courtesy of the sender. Selections will be made for review in the interests of our readers and as space permits.

ATLAS TO ANAESTHESIA. By Major Victor Cockburn, L.R.C.P. M.R.C.S. D.A. R.A.M.C. London, Baillière, Tindall and Cox, 943

SURGERY OF THE AMBLYOTIC P. THERY. By L. Kreyer, Ferguson, A.B., M.D. F.A.C.S. Philadelphia, London, and Montreal J. B. Lippincott Co. 942

THE PRINCIPLES OF NEUROLOGICAL SURGERY. By Loyd Davis, M.S., M.D. Ph.D. D.Sc., (Hon.) ed ed Philadelphia, Lea & Febiger, 942

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the tumor, in the hilus of the salivary glands—where the latter were available—and among the nodules of tumor tissue in recurrent lesions. Multiple blocks of tissue were then cut from the tumors, the salivary glands, and the lymph nodes. These were placed in a 10 per cent solution of formaldehyde, sectioned at 10 microns on a freezing microtome, and stained routinely with hematoxylin and eosin. In selected cases van Gieson's stain and Galantha's stain for mucus were employed, and paraffin blocks were used. In all, some 400 sections were thus made available for study.

PATHOLOGICAL DATA

Because, as will be shown later, the incidence of recurrence depended more on the microscopic character of the lesion than on the type or the duration of symptoms, we propose first to consider the pathological features of salivary glands tumors so that a better understanding of the clinical picture may be obtained.

From the standpoint of gross examination these neoplasms were all unilateral. Size varied from extremes of 0.5 to 10 centimeters, with an average of about 3 centimeters in mean diameter. Among the primary lesions all were unicentric except 4 which appeared as multiple nodules. Among the 28 recurrent lesions, practically all by contrast appeared as multicentric masses. Encapsulation was the rule in the majority of primary lesions examined, but the thickness of the capsule did not appear to bear much relationship to the size of the lesion or to the duration of clinical symptoms. Bosselations of the capsule were observed in 62 cases, the tumor in the remaining cases being more or less globular in shape. In 5 instances, in which the tumor was small, it appeared situated deep in the substance of the submaxillary gland. In all other instances in which the tumor was primary and in which the gland was present, the gland appeared to be spread out over the surface of the neoplastic nodule. Although it was loosely attached in most areas, nevertheless in almost every instance the gland at one or more points could be separated from the tumor only with difficulty. This observation was made so often that sections were always made, very carefully, through such adherent portions, for microscopic study.

Surfaces made by cutting revealed a somewhat variable picture. Color ranged from white to dark brown, with occasional zones of cyst formation and hemorrhage. Actual necrosis was rarely observed. Consistency varied also, but in general the whitish tumors were firm and the darker ones were soft in texture. The presence of cartilaginous tissue was noted grossly in 10 instances, and in 2 of these cases the entire tumors resembled lumpy masses of homogeneous cartilage.

In the recurrent tumors, in addition to the presence of multicentric nodularity as previously noted, it was also observed that infiltration was the rule instead of the encapsulation that had been noted in connection with the primary lesions. Probably of equal significance was the fact that in most of the recurrent lesions all or part of the submaxillary gland was present and frequently was adherent to the recurrent mass of tumor tissue. The significance of this observation will be brought out subsequently. Regional lymphatic nodes were usually present when the operation had included resection of the salivary gland. These nodes, although they were occasionally adherent to the tumor, were not obviously involved, except in some cases in which the condition was atypical, to be discussed under the miscellaneous group later in this paper.

In addition to this general gross description, certain individual cases presented features of interest. Among the group listed as "primary tumors" were 6 melanoeitheliomas. Four of these were so deeply pigmented that diagnosis could be hazarded merely on the basis of gross inspection. The tumors involved the regional lymphatic nodes, whereas the gland itself remained free. Although interesting from the standpoint of gross pathology, these melanotic lesions were excluded from the present study because in no instance could we rule out their metastatic nature. (In 2 the eye very probably was the site of the primary lesion.) Tumors of an obvious papillary nature were found in 3 instances and in 2 of these the regional nodes were grossly involved. An unusual appearance was noted in 1 recurrent tumor which presented a gross picture resembling that of a group of uterine fibroid tumors. This tumor proved to be a rhabdo-

of some of the older conceptions regarding the nature of mixed tumors. The occurrence of such tumors elsewhere than in the salivary and lacrimal glands has simplified the problems of histogenesis. Reports of regional and distant metastasis have forced many investigators to question the benignancy of these tumors. This gradual change in the pathological concept is perhaps best illustrated by the observations of McFarland (9) an outstanding authority on the subject of mixed tumors. Reporting on a large series in 1926 this author concluded, among other things, that mixed tumors are inherently benign but commonly recur after excision and if frequently disturbed become locally destructive and invasive without giving metastasis. The same author (10) writing in 1933 stated on the basis of an augmented series in which prolonged postoperative observation was carried out "Recurrence makes it certain that the [mixed] tumors are malignant in themselves, and not by virtue of carcinomatous or sarcomatous degeneration."

It is thus, in a general way, that we wish to introduce our subject of tumors of the submaxillary gland. No attempt will be made herein to review in detail the volume of information written on these tumors. For this the reader is referred to the excellent articles written by Wilson and Willis, Wood, Fry, MacFee, Harvey, Dawson and Innes, Fraser, Albhorn, New, and others in addition to those mentioned previously.

PURPOSE OF STUDY

The difficulties encountered during operation on the submaxillary gland are slight in comparison to those that must be met in operation in the parotid region. Mixed tumors of the parotid gland have a tendency to recur and most investigators are ready to admit that such recurrence obtains on the basis of incomplete removal of the original tumor rather than the result of independent neoplasia. Difficult and often inadequate exposure through the tense parotid fascia often results in rupture of the capsule of the tumor and una voidable soiling of the operative field with tumor cells. The intimate proximity of branches of the facial nerve and of other structures makes the sure way of excision instead of enucleation of

the tumor—a tumor considered by many to be slowly growing and benign.

In the submaxillary region where the same types of tumors occur the diagnosis can be made early, the surgical approach is usually simple, and complete removal of the tumor should be a matter of small difficulty. Consequently recurrence of submaxillary mixed tumors should be rare. Observation of a patient who did have such a recurrence prompted us to undertake investigation of the problem we have mentioned briefly with the following questions in mind:

1. Are all submaxillary tumors of "mixed type?"
2. Are mixed tumors benign or malignant?
3. Why do certain submaxillary mixed tumors recur?
4. What surgical procedures for eradication of these tumors are attended with the best results?

An examination of the literature revealed that submaxillary tumors, because of their extreme rarity, had been reported either singly or in small groups. It was therefore conceived that something of value might be learned from the study of a large series.

MATERIALS AND METHODS

Records of some 300 patients suffering from "submaxillary malignancy" were reviewed and carefully analyzed from clinical, surgical and pathological standpoints. More than 80 per cent of these tumors were found to represent metastatic lesions metastasis usually having taken place from epidermoid carcinoma of the lip, nasopharynx or face. Such tumors were excluded from the present study. Records of the rest of the cases (about 90) were carefully abstracted with special reference to necessary clinical and surgical data and end results. The pathological material available in practically every case was then obtained and was studied in gross detail. In each instance the tumor was drawn to scale and its size, contour and color were noted. The relationship of the tumor to the salivary gland was checked, especially in the matter of the ease or difficulty with which the tumor could be separated from the glandular substance. Regional lymphatic nodes were sought in the tissue surrounding

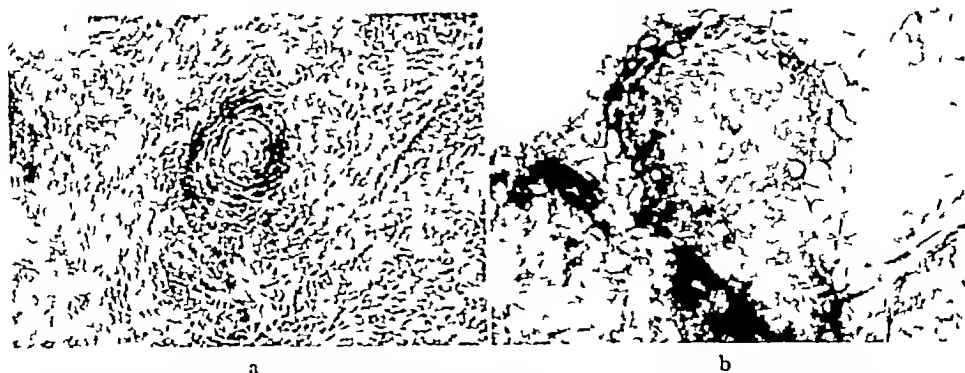


Fig 3 a, Grade 1 adenocarcinoma mixed tumor type in which an area of squamous cell metaplasia appears (hematoxylin and eosin $\times 170$), b grade 1 adenocarcinoma mixed tumor type in which invasion of fat is evident (hematoxylin and eosin $\times 45$)

study under low magnification that the epithelial cells were giving rise to the stromal cells, or vice versa.

Although the epithelial cells usually were disposed in the form of solid strands and masses (Fig 1b), very frequently they were arranged in alveoli, acini or tubules with the production of a picture approaching that of the normal submaxillary gland. These glandular spaces were frequently filled with a material which stained intensely red with eosin, and this same material gave a slightly positive reaction to the Galantha stain for mucin (Fig 2a).

The lining of these ducts and alveoli, strangely enough, was composed of two layers of epithelial cells—a superficial layer and a basal layer. In both layers the cells were small, cuboid, with large hyperchromatic nuclei and relatively large nucleoli (Fig 2a). This reduplicated lining was comparable to that found in the submaxillary duct (Fig 2b) and its radicles, and would seem to favor the theory of the epithelial (and glandular) origin of these tumors. The cellularity and activity of the epithelial elements varied, although not considerably. The malignancy of the tumors was such that 41 were classified as being of grade 1 and only 10 as being of grade 2, on the basis of cellular dedifferentiation (Broders' method). Mitotic figures never abundant were found in 8 of the tumors in each grade. Additional noteworthy features as applying to the epithelial elements were the finding of squamous cell metaplasia in 14 instances (Fig 3a) and inva-

sion of islands of capsular fat in 3 instances (Fig 3b). In no case could an actual point of origin from salivary glandular epithelium be proved, but the gross observation of regional tumor attachment was confirmed microscopically. (It may be readily seen from the appearance of the section in Figure 4 why separation of these tumors by "simple enucleation" cannot be effective in all cases, and why "recurrence" is more to be expected than non-recurrence in cases in which the submaxillary gland is allowed to remain. When only simple enucleation is carried out a few tumor cells remain at the points of attachment between tumor and gland. Such regional invasion of the capsule was observed in 18 instances and it explains we believe the multicentric origin of recurrent lesions.)

The stroma varied even more than did the epithelium, both in quality and amount. Hya-



Fig 4 Grade 2 adenocarcinoma mixed tumor type showing close attachment of tumor to submaxillary gland. Shelling out would have resulted in recurrence. In later months changes in clinical behavior and response to treatment.

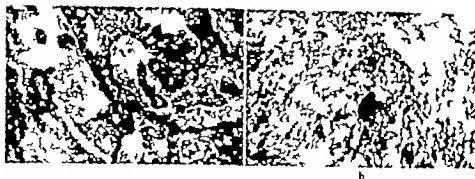


Fig. 1. a, Typical grade adenocarcinoma, mixed tumor type, in which irregular anastomosing strands of closely packed dark-staining cells can be seen between the strands are masses of hyaline and myxofibrous stroma (hematoxylin and eosin $\times 45$). b, grade adenocarcinoma, mixed tumor type in which epithelial cells are seen to fuse with the myxomatous and cartilaginous stromal elements (hematoxylin and eosin $\times 70$).

myosarcoma. Five lipomas were found in the collection, and had typical gross appearances as did also an epidermoid carcinoma arising deep in a sebaceous cyst. These 6 last tumors were excluded from the study but were of interest from the standpoint of differential diagnosis. Through a process of exclusion, therefore, 81 cases finally formed the basis for the analysis herein submitted.

In the microscopic study of these lesions it was soon discovered that the tumors labeled "mixed" could be very conveniently divided into four groups: (1) adenocarcinoma—mixed tumor type 51 cases; (2) adenocarcinoma—cylindroma type 15 cases; (3) adenocarcinoma—intermediate form (1) and (2) 7 cases; (4) miscellaneous, 8 cases.

Group 1. The picture in group 1 was that of irregular masses and strands of closely packed small epithelial cells with practically no intercellular stroma (Fig. 1a). Between these masses, however, were zones of fibromyxomatous tissue which varied from hyaline on the one hand (Fig. 1a) to a substance identical with cartilage on the other (Fig. 1b). In addition, the relationship of the epithelial to the stromal elements varied considerably even in the same microscopic section. In some areas there appeared to be definite lines of demarcation between epithelial and supporting cells; in others, the 2 elements seemed to fuse imperceptibly one with another. The latter occurrence was especially true in the central parts of tumor nodules, where it would seem from



Fig. 2. a, Grade adenocarcinoma, mixed tumor type, in which formation of acini and tubules lined by double layer of epithelium can be observed and in which the resemblance of these differentiated ducts to the normal subcutaneous duct depicted in Figure 2b is evident. One of the acini is filled with mucus (hematoxylin and eosin $\times 275$). b, Normal subcutaneous duct, in which superficial and basal layers of epithelium being are evident (hematoxylin and eosin $\times 35$).

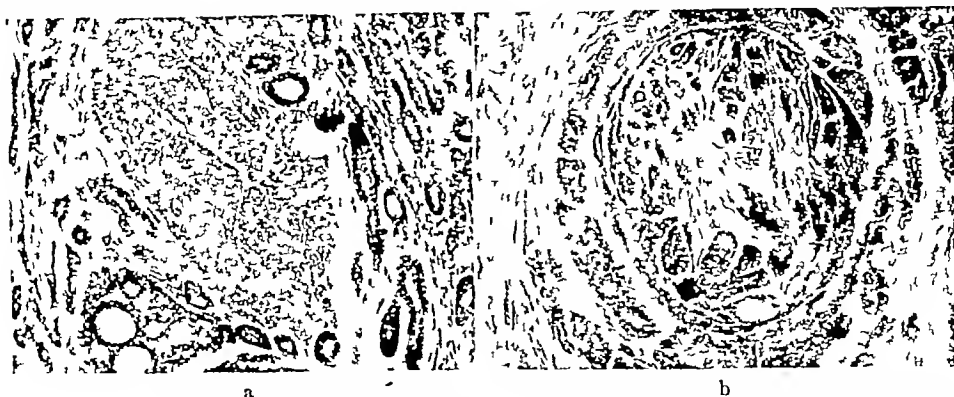


Fig 7 a, Grade 2 adenocarcinoma, cylindroma type, showing invasion of perineural lymphatic structures and actual invasion of the nerve bundles (hematoxylin and eosin $\times 70$), b, grade 2 adenocarcinoma, cylindroma type veritable "carcinomatous neuritis" (hematoxylin and eosin $\times 70$)

changes observed were the presence of inflammatory (lymphocytic) infiltration in 10 cases (Fig 4) and metaplasia of ducts observed on 1 occasion. Regional lymphatic nodes were identified microscopically in 14 of the specimens. Only 2 instances of involvement were found, once in a primary lesion and once in a recurrent lesion. This observation is in keeping with the known facts concerning mixed tumors.

Group 2 In group 2, the purely cylindromatous type of tumor, the microscopic picture was that of honeycombed cylinders or plugs of small, dark-staining epithelial elements in a hyaline stroma (Fig 5a). As in the true mixed tumor, the cells were cuboid, with large, hyperchromatic nuclei and scanty cytoplasm (Fig 5b). Mitotic figures in general were more

abundant, and the average grade of malignancy appeared to be higher than in the mixed tumor group. Using the method of Broders, we found that 2 of the tumors were grade 1 and 12 were grade 2 carcinomas, and 1 was grade 3 carcinoma.

The characteristic honeycombing seen on microscopic section appeared to result from a grouping of epithelial elements around true and pseudoacini. In the former the acinar spaces appeared to be filled with a substance which stained positively for mucus, in the latter the spaces were usually empty and the lining cells had irregular luminal margins. In this group there was in general considerable evidence of origin from duct epithelium, particularly from the basal layers. In several instances foci of neoplastic growth were found in



Fig 8 a Grade 2 adenocarcinoma, cylindroma type, showing infiltration of muscle (hematoxylin and eosin $\times 45$), b grade 2 adenocarcinoma, cylindroma type, metastasis to regional lymphatic node is shown (hematoxylin and eosin $\times 70$)



Fig 5 a, Adenocarcinoma, grade 1, cylindroma type, in which the honeycomb arrangement of epithelial cells grouped in tubular pattern of architecture and large amount of hyaline stroma are evident (hematoxylin and eosin $\times 34$). b, Adenocarcinoma, grade 2, cylindroma type, in which true and pseudoglandular arrangement of closely packed and dark-staining tumor cells are observed. The cytoplasm is scanty and nuclei thus stand out very prominently (hematoxylin and eosin $\times 3$).

line connective tissue was found in 45 cases and was sometimes present in broad sheets. It was especially prominent in the tumors which were grossly described as being "hard" (34 cases). Cartilage was present 37 times and in 10 instances constituted the bulk of the tissue microscopically. Myxomatous degeneration was observed in 32 of the tumors, but in some instances origin from epithelial mucus could not be entirely excluded. Areas of calcification were found in 10 instances and osteoid tissue was observed once. True formation of bone however was always lacking. Peripherally the connective tissue of the stroma was usually

condensed to form a capsule. Such condensation was demonstrated in all the primary tumors, but was absent in 8 of the 11 recurrent lesions. Tumor capsules varied greatly in thickness, and occasionally were incomplete. As stated previously in 18 instances there was invasion by epithelial tumor elements. In 10 cases ductule-like structures were present which probably were of salivary glandular origin. In 16 cases the capsule was adherent to the gland at multiple points and in no case in which the gland was available could it be considered as being entirely separate from the tumor. In the gland itself the only noteworthy



Fig 6 Submaxillary gland as seen at distance from the main body of the tumor. an adenocarcinoma, cylindroma type is growing around duct. Whether this represents origin or extension is questionable but in either case the observation serves as an argument for radical surgical removal (hematoxylin and eosin $\times 103$). b, Adenocarcinoma, grade 2, cylindroma type, in which the intimate relationship of the glandular to the tumorous elements is evident (hematoxylin and eosin $\times 70$).

considerably greater than is the case with mixed tumors. In both, however, it appears to be a relatively late phenomenon.

Group 3 The intermediate group was small and merits little in the way of special comment. Suffice it to say that the neoplasms microscopically exhibited the characteristics of the mixed and the cylindromatous patterns, so that separate classification seemed justifiable. The incidence of recurrence was higher in this group than it was in the mixed group, and the microscopic picture of the recurrent nodules tended to reproduce the cylindromatous fraction of the original lesion with invasion of nerve sheaths in 6 of the 7 cases (Fig 9).

Group 4 In the miscellaneous group was a number of tumors which were difficult of classification. In 3 instances the salivary gland appeared to be the seat of a primary papillary adenocarcinoma, and in 2 of these the regional lymphatic nodes were metastatically involved. In 2 cases the tumors were examples of primary (?) squamous cell carcinoma of the submaxillary gland, either by direct origin or through metaplasia in a pre-existing mixed tumor. In 1 case a grade 1 mixed tumor and a grade 4 adenocarcinoma were found in separate nodules of the same lesion (Fig 10a and b). The nodes were involved metastatically by the high-grade lesion. In 1 case the primary submaxillary neoplasm was rhabdomyosarcoma which promptly recurred after removal. There was no evidence that it was glandular in origin. One of the tumors was of the nature of an epignathus.

CLINICAL DATA

Incidence The incidence of mixed tumors was approximately one in every 20,000 clinic admissions (51 cases among slightly more than 1,000,000 patients). Such an incidence is considerably lower than that reported by Stein and Geschickter, who in a recent large series recorded 1 mixed tumor in every 208 hospital admissions, with submaxillary tumors constituting 10 per cent of the entire group. Adenocarcinomas of the cylindroma type constituted 18 per cent of the entire series of 81 cases. This figure agrees well with that of the group reported by Stein and Geschickter, in

which "adenocystic basal cell carcinomas" comprised 17.4 per cent of a series of 241 cases. Seven, 8.7 per cent, of our cases were of the intermediate group and 8, 10 per cent, were classified as "miscellaneous."

Sex of patients It is generally stated in the literature that mixed tumors show no predilection for persons of either sex. In the present series mixed tumors occurred 31 times in females and only 20 times in males. In addition, in 9 of 11 cases recurrence took place in females. Cylindromas afflicted 10 females and only 5 males. In the intermediate and miscellaneous groups the tumors were found to have a 2:1 preponderance for the male sex.

Age of patients Stein and Geschickter and others have pointed out that mixed tumors occurred among young persons and that cylindromas occurred among middle-aged persons. According to McFarland (10), 50 per cent of mixed tumors occurred among persons between the ages of 20 and 40 years, the peak of incidence being noted late in the third decade. In the present series of 51 mixed tumors, 46 per cent of the patients were between 20 and 40 years of age, the average age for the entire series being 39 years. The youngest patient was 12 years old and the oldest was 79 years old. Of the 15 patients who had cylindromas, 11 were between 40 and 50 years of age, the youngest was 27 years old and the oldest was 76 years old. The average age in the "intermediate" group was 48.7 years and in the "miscellaneous" group it was 44.4 years. In the former group the majority of the patients were in the fifth decade and in the latter group, the sixth decade. Recurrence was related to the age of the patient only in the mixed tumor group, where the average age of patients who had recurrent lesions was 32 years, or 7 years less than the average for the group in which no previous operation had been performed. Family and personal histories were carefully scrutinized in every instance for possible clues as to the etiology of these tumors. Results of such investigation were, not surprisingly, fruitless.

Symptoms The only constant symptoms complained of was the presence of a tumor, and this complaint was elicited in all except 2 cases in which "discovery" of a tumor was



Fig. 9. Grade 4 adenocarcinoma, from the intermediate group. Note again the tendency toward invasion of nerve bundles (hematoxylin and eosin $\times 34$).

the submaxillary gland at a distance from the main body of the tumor (Fig. 6a). In fact these tumors, in general, exhibited a more intimate relationship to the salivary gland than did neoplasms of the true mixed type, a relationship which on the basis of our observations could not be entirely explained on the basis of direct extension (Fig. 6b).

The stroma of the cylindromas, although it was not so variable as in the case of mixed tumors, was nevertheless fully as characteristic. In general it was fibrous or hyaline and usually large in amount. Usually concentrated in zones between the islands or nests of epithelium, in many cases it was intracellular compressing and sometimes almost fusing with the cytoplasm of the parenchymatous cells (Fig. 6b). In such instances the epithelial

cells appeared to be small and atrophic, and the irregular anastomosing bands of hyaline stroma presented a mosaic pattern that was highly characteristic.

Perhaps the most important observations made in this entire series of tumors were the infiltrative tendencies of tumors of the cylindroma group. Capsular invasion was observed almost regularly. Infiltration of the salivary gland was commonly found, this infiltration being particularly evident in the periductal lymphatic spaces. But perhaps of greater importance was the pronounced tendency of the tumors to grow in perineural lymphatic spaces (Fig. 7a). In some instances there was actual invasion of nerve bundles—veritable carcinomatous neuritis, so to speak (Fig. 7b). In the cases in which the tumors were recurrent the reappearance took the form of multiple nodules and almost invariably within these nodules the process of nerve involvement appeared as a sort of nucleus. Even in primary tumors, nerves in the capsule often were invaded. In the later stages, especially in recurrent lesions, muscles and adipose connective tissue also exhibited malignant invasion (Fig. 8a). In our opinion this was probably secondary to perineural spread of the disease.

Regional lymphatic nodes were identified in 9 of the 15 cases. In 4 instances these were involved by carcinoma (Fig. 8b). In all 4 cases the lesions were examples of recurrent neoplasms. The tendency of cylindromas to involve lymphatic nodes appears therefore to be

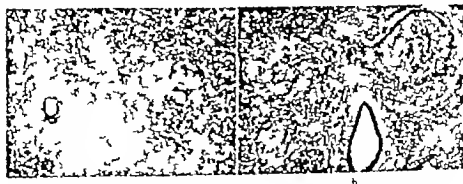


Fig. 10a and b. Combinations of grade 4 adenocarcinoma, mixed tumor type (left) squamous cell metaplasia and grade 4 adenocarcinoma. Both lesions are found in the same tumor nodule (hematoxylin and eosin $\times 70$).

the miscellaneous group of cases as previously detailed. The right side was involved 43 times and the left side 38 times. Bilateral involvement was not observed.

McFarland (11) has pointed out an apparent paradox in connection with the size of surgically removed mixed tumors. This author, referring chiefly to parotid tumors, stated that small tumors recurred more frequently than did large ones. In the present series the average diameter of the lesions was 3.1 centimeters. Data on the size of tumors were not available in the 11 cases in which operation was performed for recurrence. However, 10 patients who had primary mixed tumor were living 5 to 20 years after operation (at the time of our report) and in each the diameter of the tumor was less than 1.5 centimeters. It may be possible that the performance of conservative "enucleation" has been responsible for the reported high rate of recurrence of small tumors. There was no evidence in our series that "ripening" of the tumor was related to age of the patient or indeed to magnitude of the lesion. In the cylindroma group the average size of the lesion was 4.5 centimeters, the average size of the primary lesion being 2.8 centimeters and that of the recurrent lesion being 5.4 centimeters. In the "intermediate" group tumors averaging 4.4 centimeters were presented, and miscellaneous tumors averaged 4.7 centimeters in diameter.

Surgically, cases of mixed tumor were divided into those in which a primary tumor was presented and those in which the neoplasm was recurrent. For 38 of the 40 patients who had primary mixed tumor all or part of the submaxillary gland was surgically excised, along with the neoplasm. Eight of the 40 patients were operated on recently, and recurrence may or may not develop. Of the 32 remaining patients, 3 died of causes unrelated to their submaxillary lesions, 21 were living without recurrence from 4 to 25 years after operation (at the time of this report), whereas the 8 remaining patients have not been heard from. Of the 11 patients who had recurrent lesions, 5 were seen and treated too recently to permit final analysis to be made. Of the 6 remaining patients in this group of 11, 1 died of renal insufficiency 16 years after operation.

There had been no return of the lesion. For 4 patients arrest of the carcinoma was effected for periods varying from 4 to 10 years. The sixth patient suffered recurrence nine times over a period of 10 years, and was last heard from in 1934.

We believe it to be of some significance that all or part of the submaxillary gland was present in 9 of the 11 patients who came to the clinic for treatment of recurrent lesions, indicating that a conservative type of primary operation had been performed. Although a second operation appeared to eradicate the disease in nearly all instances, it is believed that primary radical surgery would have furnished some insurance against recurrence of the lesion.

In the group of cylindromas the tumor was primary in 5 and recurrent in 10 instances. In all cases in which the lesion was primary, gland and tumor were removed *en bloc*. One of the patients was living 26, and another 5, years after operation at the time of this report. The rest succumbed from recurrence of metastasis, 2 of them died in spite of repeated operations. In the second group 1 patient was living, at the time at which we write, 5 years after operation for a second recurrence. Two patients were treated recently and cannot be included in a statistical analysis of end-results. Concerning 2 patients we have no data other than that they were suffering from recurrence when they were last heard from. The 5 remaining died from carcinoma. In all but 2 of the recurrent tumors it was possible to find remnants of the submaxillary gland and it is possible if not probable that in these cases also the original "tissue sacrifice" had not been adequate.

In the "intermediate" group of neoplasms, tumor and gland had been removed in 4 instances. Two of the patients were living 20 and 4 years, respectively, after operation, at the time of this report. In one the gland was extensively infiltrated, and this patient succumbed in a year to spinal metastasis. Another died from recurrence in 15 months. In 3 instances only a part of the gland was removed. Two of these patients died from recurrence. We have no subsequent data on the third patient.

made during the course of examination. Among patients who had mixed tumors, the average duration of this symptom was 7 years when the tumor was primary and 4.7 years when the neoplasm represented a recurrence. Extremes of 40 years and 1 month were found. Among the 11 instances of recurrence in this group the average time elapsing between the first operation and the onset of the recurrent lesion was 2 years, with extremes of 6 months and 7 years. The average time elapsing between the first instance of recurrence and the second operation was 3.8 years. These figures, although they are based on a small number of cases, tend to indicate that the more rapidly growing tumors are the ones which usually recur. The evidence shows on the other hand that the behavior of the primary tumor does not necessarily serve to predict the behavior of the recurrent lesion.

In the cylindroma group 5 of the patients came to the clinic for consideration of their primary lesion. In this small group the average duration of symptoms was 3 years, with extremes of 6 years and 6 months. Of 10 patients who came for treatment of a recurrent tumor the average duration of the primary symptoms had been 5.6 years, with variations of from 12 years to 1 year. The duration of the recurrent lesion on an average was 1 year.

In the "intermediate" group only 1 patient came to the clinic for the treatment of a recurrent tumor. This person had had primary symptoms for a year and recurrence took place 18 months after operation. The average duration of the swelling in the remainder of cases was 6.3 years (4 years, if we disregard 1 case in which the duration was unusually long, 30 years). The shortest duration of the swelling was 6 months.

In the group of miscellaneous cases 3 patients presented themselves with primary lesions. One patient gave a history of the presence of a "lump for 20 years" and was free from recurrence after 7 years at the time of our writing. In another patient the tumor had been present for 50 years, but it had grown very rapidly for 6 months. This patient succumbed within 2 years, death being caused by the unusual combination described herein in the section called Pathologic Data—a grade

4 adenocarcinoma engrafted on a grade 1 adenocarcinoma of the mixed tumor type. The third patient who had a 6 month history was living at the time of this report, with recurrence after 2 operations for the removal of a grade 2 papillary adenocarcinoma had been carried out.

Of the 5 patients presenting themselves for treatment of a recurrent neoplasm of the "miscellaneous" type, 4 had short histories, and there was a rapid return of the neoplasm after removal. One of these patients died after a second recurrence, 1 was treated only recently and 2 have not been heard from. In the fifth case the diagnosis was epiglottic tumor and the patient probably is living and well at the time of our report.

Pain and tenderness. A perusal of the literature on mixed tumors leaves one with the impression that pain is not an outstanding symptom. This observation was confirmed in the present study. Only 4 of the 51 patients complained of pain and tenderness in the region of the tumor and in no instance was either severe. In the cylindroma group, however, pain was a prominent feature in 11 of the 15 cases. Pain usually was moderate in severity and of shorter duration than the swelling. It appeared to be more or less directly related to fixation of the tumor clinically and pathologically to involvement of nerves. This rather high incidence of pain we believe may be of importance in the making of a correct preoperative diagnosis.

In the intermediate group, pain was not a common symptom. It was present in 3 cases, in 2 of which extensive microscopic invasion of nerves had occurred. In the miscellaneous group of cases pain was present in only 2 of the 8 patients.

Miscellaneous symptoms, not previously mentioned herein occasionally were encountered but did not appear to be of diagnostic significance. In a number of instances the tumor was said to fluctuate when the patient caught cold, and in 4 instances the tumor was first noted after attacks of tonsillitis. In general growth of the tumor was steady but in 8 cases there was a history of an accelerated rate of growth which however did not appear to be of serious significance except in 1 case.

was extremely high, and the outlook generally unfavorable

4 An "intermediate" group of cases was found in which the tumors pathologically shared the features of the mixed tumors and the cylindromas. Clinically, also, the histories of the patients justified separation of the tumors into a special category

5 Eight patients, 9.5 per cent, had atypical tumors described as "miscellaneous." Prognosis depended partly on the type and grade of the lesion and partly on the extent of lymph nodal involvement

6 Clinical follow-up studies have demonstrated the usefulness of the microscopic classification we have presented, in relation to prognosis

7 Throughout the study we were impressed by the disappointing results which followed conservative operation on malignant tumors of the submaxillary gland

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In the miscellaneous group at least remnants of the submaxillary gland were found in all 4 recurrent tumors indicating that a conservative operation had been performed for removal of the primary tumor. Results were better in the 4 remaining cases in which gland and tumor were included in the operative resection. Throughout the entire series it may then be stated that the best results were obtained when in the primary surgical operation the submaxillary gland was removed. The difference in end-results in this particular respect was fairly striking in all groups except the group of cylindromas. The discrepancy in this group is probably to be explained by the fact that the tumors frequently infiltrated even beyond the confines of the gland itself.

RESULTS OF STUDY

Before this problem was undertaken we shared what we believe to be a general impression, namely, that all submaxillary tumors are mixed tumors and of a low grade of malignancy. Nearly all of our earlier cases were so labeled and in these cases the rate of recurrence seemed unduly high. Not until we had reviewed the macroscopic pathology did it become apparent that the term "mixed tumor" indeed covered a multitude of sins so to speak. Many were cylindromas which had produced no unusual features in the clinical history (except for a high incidence of pain) but which did produce an entirely different outlook from the standpoint of ultimate recovery of the patient. To be sure 7 cases belonged to an "intermediate class," but even in this class "cylindromatous" features usually predominated to such an extent that a separate grouping seemed advisable. A miscellaneous group was created to include tumors not belonging to the types we have just listed.

On the basis of this classification we are in agreement with Ewing and McFarland (11) that true mixed tumors are of epithelial origin and that they are inherently malignant—adenocarcinomas of low grade. We have shown that recurrence of these mixed tumors is not uncommon, particularly when in the surgical attack the tumor is "enucleated" a procedure which frequently leaves tumor cells behind. We have seen that removal of a recurrent

tumor is not so successful as performance of a complete primary radical procedure from the standpoint of avoidance of further involvement. It is felt, furthermore, that the surgeon cannot possibly distinguish at operation the simple mixed tumor from the highly dangerous cylindroma in which recurrence frequently follows, even after radical operation for removal of the primary lesion. For these reasons we are in complete disagreement with those who advocate local enucleation for submaxillary tumors. The disease can be thoroughly eradicated only by removal of the tumor en bloc, the salivary gland and the regional lymph nodes. In the case of the cylindroma even this procedure may not be effective. Microscopic extension beyond the limits of gross invasion has been repeatedly demonstrated in our cases, this extension having a peculiar affinity for perineural lymphatic structures. (Existence of the perineural spread of carcinoma has been known for years, but it has not received the attention it deserves. It was emphasized by Kahler in a recent paper on carcinoma of the prostate gland.) In the intermediate and miscellaneous groups of tumors as we have classified them, the prognosis is only fair but to these groups, again, the same surgical principles should apply and the surgeon should not be deceived by apparent encapsulation of the tumor.

SUMMARY

1. Eighty-one primary submaxillary malignant tumors have been reviewed from the clinical and pathological aspects.
2. True mixed tumors constituted 63 per cent of the series. They represented low grade slowly growing adenocarcinomas usually not associated clinically with pain or local fixation. The tendency toward recurrence was not pronounced except when inadequate "tissue sacrifice" had been carried out.
3. Adenocarcinomas of the cylindroma type accounted for 18.5 per cent of the tumors. These cylindromas as a rule were associated with a short clinical history in which pain and local fixation were prominent features. Pathologically the lesions, although they were of a moderate degree of malignancy presented pronounced infiltrative tendencies with selective invasion of nerves. The rate of recurrence

skin incision should be covered with laparotomy sponges or towels carefully. If it could be remembered that the surface of the skin, only, has been rendered free of live organisms, not its deeper layers, nor the hair follicles, the sweat glands nor the sebaceous glands, more rigid protection would be diligently carried out in protecting the delicate peritoneal surfaces from these ever present dangers of bacterial contamination. It is well understood that trauma must take place to peritoneal surfaces no matter how gently the manipulations are carried out. That trauma can be minimized by gentler handling, gentler packing off of viscera, gentler retraction of the parietal peritoneum and viscera, is easily understood, especially when one realizes that the peritoneum is nothing more than a single layer of delicate flattened cells with a very delicate basement membrane. It can offer not a whit of resistance. The peritoneum cannot resist exposure to air for many moments without drying. Drying produces death of this delicate surface rapidly as proved long ago by Walthard. He advocated soft, warm, moist gauze packs as a preventative. These should be changed frequently to prevent cooling. In order further to minimize trauma, both Coffey and Gellhorn object to the use of gauze packs, moist or dry, and advocate thin rubber sheeting instead. The modern rubber glove is an excellent agent to employ in the handling of viscera. When moistened with warm saline it is difficult to conceive that many pavement cells are devitalized by its gentle application. Instruments of steel are difficult to devise in order to make them trauma proof. They are usually too rigid, toothed, corrugated, or lined too deeply. The hemostat, the Allis forceps, the usual run of thumb forceps, smooth or toothed, and even the Percy-Allis forceps are mentioned only to be condemned. A rubber-covered thumb forceps, the resilient type of Babcock forceps or its modification advocated by one of us (17) may be employed assuring a minimum of trauma—yet trauma nevertheless.

Many cases of postoperative adhesions can be attributed to poor operative techniques other than those which have been mentioned. Most glaring of them all is the peculiar

practice of neglecting to peritonealize injured, lacerated, or crushed surfaces. It has been the visual experience of many in the past to have witnessed this grave omission. Apparently, the guilty operator has inherent faith in the ability of the peritoneum to withstand not only the extensive trauma of the operative procedure at hand but also that it will always be able to "cover up," his errors of denudation, laceration, and cut surfaces.

Much research and clinical experimentation has been carried out in the past generation in an effort to guard the peritoneal cavity against the formation of adhesions as well as to guard it from postoperative infections. The scope of this paper is too limited to attempt a discussion of the numerous prophylactic agents employed. A number of them have enthusiastic clinical, as well as research, reports to substantiate them.

THE ATTACHED OMENTUM

The ubiquitous omentum has not received the support it should as an agent in adhesion prevention. There are many uses to which it may be harnessed. Mann advocates its use in adhesion prevention, as do Sweet, Chaney and Willson (23). The latter group carried out a long series of excellent experiments with free and attached omental grafts. Springer also used attached omentum freely. Many good surgeons use attached omentum to cover the repair of ruptured peptic ulcers, the damaged areas following cholecystectomy and choledochostomy. Over intestinal anastomoses, duodenal stumps, denuded parietal or visceral peritoneum, around enterostomy tubes, beneath abdominal incisions, the omentum is freely employed to good advantage. In checking hemorrhage from parenchymatous organs, Loewy suggests its use in liver, spleen, and kidney damage. Clark and Byford, however, warn against its use because its attachment to the denuded or inflamed area may interfere with normal physiology of the stomach and transverse colon. This may be true especially in its use in pelvic denudations or infections. Pirone, Wilkie, and Bost recommend, and have used, attached omentum as a "wrapping" about a strangulated portion of the intestine the viability of which

THE FREE OMENTAL GRAFT

A Clinical and Experimental Study

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THE past generation has witnessed a tremendous increase in the number of operations within the abdominal cavity. Concomitantly ever multiplying numbers of cases of acute and chronic intestinal obstruction and postoperative adhesions have arisen with this increase. With the myriads of surgical invasions within the peritoneal cavity not only in the many large surgical centers but also in every rural hospital it is remarkable to note that the number of cases of adhesive obstruction and postoperative adhesions is comparatively and indeed very small. In a series of 511 cases of acute intestinal obstruction studied at Charity Hospital, New Orleans, over a 6 year period Moss and McFetridge found 26.8 per cent were due to adhesions. At the John Gaston Hospital, Memphis, 581 cases of acute intestinal obstruction were studied over a 10 year period by us (17) and 17.2 per cent were found due to adhesions, either inflammatory or postoperative. The two hospitals mentioned have a large general surgical service, particularly in abdominal surgery. The total number of cases of obstruction due to any cause is but a fraction of total number of celiotomies performed in comparative periods.

The reactions incident to inflammation of the peritoneum, due to bacterial invasion have played a considerable part in the cause of intestinal obstruction of the adhesive type. A large percentage of obstructions, however can be traced to traumas other than infection. The most common of these are rough handling of the viscera, too much instrumentation, poor choice of abdominal sponges and packs, exposure and drying. It is also common to

find errors in operative technique that lead to adhesions. The main offender here is the operator who does not peritonealize traumatized surfaces sufficiently, whether they be cut, crushed, lacerated, or torn.

During the past few years free omental grafts have been used in 13 cases of adhesive obstruction, and in areas of potential obstruction, where relatively large areas of denudation of visceral or parietal peritoneum resulted. In none of the cases reported have the clinical results required further abdominal surgery. In an effort to determine parallel results in animals, dogs were subjected to laparotomy, free omental grafts were applied to scarified areas, and then explored 3 months later.

THE PREVENTION OF ADHESION FORMATION

The advent of the aseptic era in surgery has done by far the most good in aiding in the prevention of adhesions after operation. In this present age of surgery, infection should not follow clean surgical cases if the usual diligent care is assumed by the operating room supervisor, her assistants, or nurses, in the routine, but ever careful preparation of the linens, drapes, sponges, and instruments. The word routine is dangerous. But eternal vigilance is the price of peace, and this vigilance requires frequent rechecks of sterilizers, temperatures, autoclave pressures, etc. Breaks in sterile technique occur among the best operating room teams. Should there be any question or doubt as to a break the very fact that there is a question or a doubt about the break, rectification should be made without any hesitation. This would be an excellent routine. It would save time, tempers, and sometimes lives. The use of skin antiseptics should be carefully guarded, as well as any other chemical compounds when the peritoneal cavity and contents are exposed. The

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Fig. 1. Case 1. a, Results of cholecystectomy 1 year previously. Hepatic flexure of colon, duodenum, and pylorus densely adherent to liver and gall bladder fossa. b,

After sharp and blunt dissection. Denudation of gall bladder fossa, liver, hepatic flexure of colon, duodenum, and pylorus. c, Free omental grafts cover all denuded areas.

which runs something like this: 'Oh I've applied free grafts now and then and I've seen Dr. So-and-So apply them. When conversation continues, and we wish to learn what happened in those patients who were subjected to the grafts, the answers become extremely vague. Witness the dearth of detailed clinical reports. The last, and only report worthy of mention is Graham's published in 1934. Excellent reports such as his probably lie tucked away, embryonically, in the cortex of many a surgeon, and in his office records. We hope the following tabulation of our 15 private patients will stimulate more than a few to put their office force to work, as we did, to help substantiate the fine experimental data of the literature on this interesting subject. We would be delighted to learn of Dr. So-and-So's experience with free grafts. Probably a summary of these collected personal observations and records could be published in a few years hence.

The authors regret that re-explorations or autopsy material have been unavailable in this series, but the clinical results have certainly proved most encouraging to us.

verse colon to the region of the gall bladder 10 sa were noted. The first portion of the duodenum was markedly contracted. Operation consisted of sharp dissection, relieving the stomach, duodenum, and transverse colon from the liver and the gall bladder fossa. Grafts were applied (1) 8 by 6 centimeters, to the liver and gall bladder fossa; (2) 10 by 8 centimeters, to the stomach and duodenum; and (3) 6 by 6 centimeters, to the transverse colon and mesocolon. There has been no recurrence of "gall bladder colic" to date. The gastrointestinal series is normal.

CASE 2. S. S., female, aged 28 years, was operated upon August 17, 1937. In 1930 she had had an appendectomy and right salpingectomy. She complained of colic like pain, nausea and vomiting. The terminal ileum was completely blocked by adhesions, the result of right chronic pelvic inflammatory disease. The left adnexa were normal. Operation consisted of right oophorectomy. A graft 10 by 6 centimeters was applied to the denuded terminal ileum. No recurrence of symptoms to date.

CASE 3. W. B., female, aged 31 years, was operated upon October 2, 1937. In 1930 appendectomy had been done. Patient complained of lower abdominal pain, nausea and vomiting, dysuria, frequent, and a loss of 15 pounds in weight during 12 months previous to admission to the hospital. There was a profuse vaginal discharge, bilateral adnexa enlarged and tender. At operation the following was noted: a chronic bilateral tubo-ovarian abscess, and the terminal ileum completely adherent to the right

is doubtful or when the patient's condition does not warrant resection. One other danger of the attached graft is that of intestinal obstruction. This may occur in one of two ways the most common, the volvulus-like loop of small bowel which becomes twisted about the omental pedicle the other the contracted "wrap" of greater omentum often seen in complete and chronic obstructions of terminal ileum or in ileocecal valve region. Binne warns against the possibility of internal hernia in the use of attached grafts.

THE FREE OMENTAL GRAFT

Senn in 1883 was the first to advocate the use of the free omental graft. Experimentally he found the grafts adhered firmly to the surfaces to which they were applied. They had become well vascularized in a very short time. He used 4 dogs in his experiments, observing his results in 36 hours to 8 days. His results were better with those grafts placed upon scarified intestine. Brocq, Ducastaing and Reilly (5) established the fact that free grafts not only were successful, but in addition that the surface endothelium of the transplanted omentum persists. Peel and Finton studied omental grafts histologically determining that in dogs the grafts survive unchanged for at least 6 months. They recommend that the thinner the graft used the better. Bennett covered a perforated peptic ulcer successfully with free grafts. Adversely Springer and Wilkie, though they do not consider free grafts unsatisfactory believe they lead to further peritoneal adhesions. Botbe in an extensive histological study found that the surface endothelium of the free graft not only persists but at the end of 2 weeks is continuous with the endothelium of the recipient organ. Sweet, Chaney and Willson found that free as well as attached omental grafts were efficacious in covering suture lines—and remain free from other adhesions. Freeman, in a purely clinical report recommends enthusiastically the use of free grafts to replace lost portions of peritoneum, to prevent adhesions to strengthen suture lines and to check hemorrhage from parenchymatous organs. Another detailed and accurate experimental report is one by

Davis, who transplanted free grafts to stomach, intestine, liver, spleen, kidney, bladder and denuded areas of peritoneum, with excellent results. He found that the grafts survived well throughout his experiments. Mann, though not very enthusiastic about free grafts, states "if however infinite care was used in handling the transplant, so that the delicate cells would not be injured, and in tucking in the edges so that none of the cut surface was exposed, it was found possible to cover a traumatized area so that few if any adhesions occurred." Graham, in 1934 presented a detailed clinical report of 20 cases of free omental grafts collected from the Methodist Hospital records in Brooklyn, New York. The grafts were used in a variety of conditions including terminal ileum, mesentery, suture line, liver and duodenum, abdominal wall defect, leaking ureter, gall-bladder fossa, and pylorus and duodenum, etc. The results warrant Graham a concluding that free omental grafts will live they are hemostatic they aid in preserving peristalsis they strengthen weak suture lines they resist infection.

In the technique of omental grafting, Freeman recommends the following. The pedicle should not be puckered by ligation the free border of the omentum should be used to avoid large vessels the graft should be carefully sutured in place with fine catgut, the transplant must extend beyond the raw surface. To these precepts should be added Mann's admonition to roll or tuck under the cut edges of the graft.

Clinical reports are still too meager concerning the ultimate fate of the omental graft. In 3 of Graham's case records was there an opportunity to examine the grafts. Although all three grafts were found intact, this number is entirely too small from which to draw conclusions containing final conviction. We must await more clinical reports which will contain data of grafts examined at re-explorations or at autopsies.

CLINICAL REPORT OF 13 CASES TREATED WITH FREE OMENTAL GRAFTS

Hardly a conversation with any surgeon, when the subject of free omental grafts is brought up, does not bring forth a statement

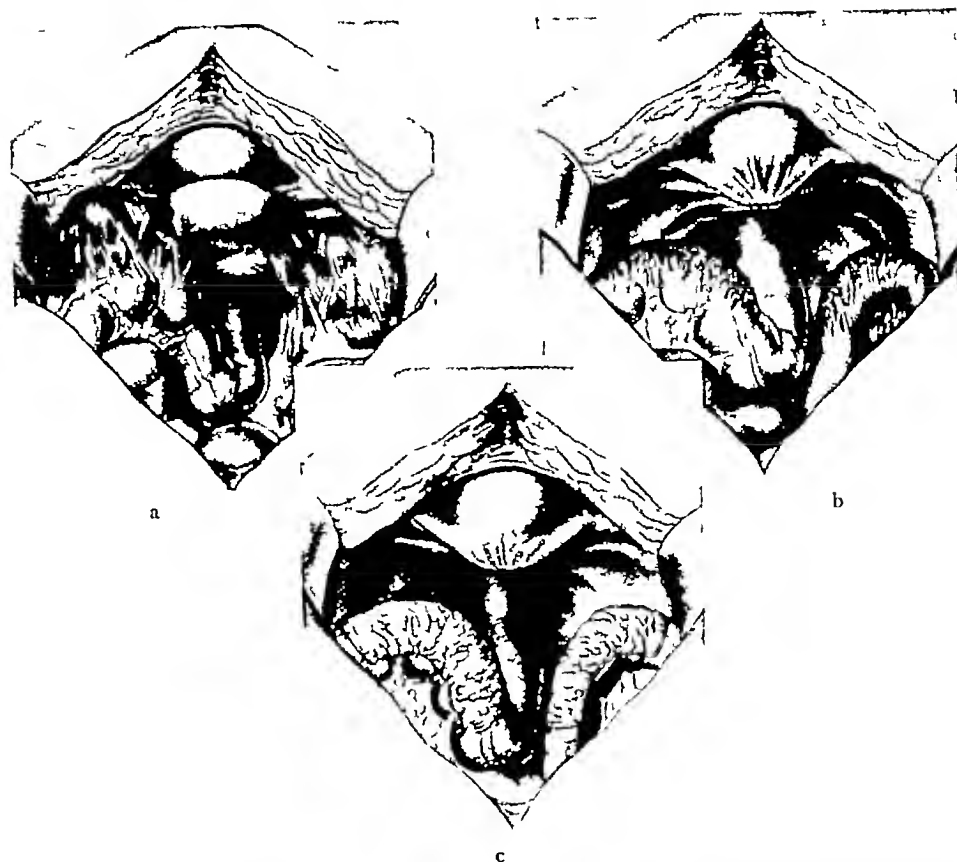


Fig 3 Case 4 a, Chronic bilateral tubo-ovarian disease Sigmoid and terminal ileum both densely adherent to adnexal masses and uterus b, Bilateral salpingo oophorectomy and supravaginal hysterectomy, complete peritonealization of lesser pelvis but denudation of sigmoid and terminal ileum c, Free omental grafts to sigmoid and terminal ileum

graft, 10 by 6 centimeters, was applied to cover the area of denudation in the left broad ligament's posterior leaf Patient made a complete recovery and has no gastrointestinal symptoms

CASE 7 L E T, female, aged 33 years, was operated upon on December 27, 1940 Patient complained of marked pain and tenderness in the right lower quadrant, of 2 months' duration A tumor was found in the lower abdomen 4 months ago A preoperative diagnosis of fibromyoma of the uterus and chronic pelvic inflammatory disease was made Operation revealed multiple myomas of the uterus, chronic bilateral salpingo oophoritis, and the terminal ileum densely adherent to right adnexa Operation supra vaginal hysterectomy, bilateral salpingo-oophorectomy, and appendectomy A graft, 8 by 6 centimeters, was applied to denuded terminal ileum Patient made complete recovery and has remained well to date

CASE 8 J A S, female, aged 41 years, was operated upon on January 4, 1941 Examination revealed lower abdominal pain, low grade fever, of 3 months'

duration, profuse vaginal discharge A preoperative diagnosis was made of chronic pelvic inflammatory disease Pathological examination revealed a right pyosalpinx, left chronic salpingitis, marked diffuse cystic degeneration of both ovaries, 12 centimeters of terminal ileum densely adherent over right pyosalpinx, and suppurative endocervicitis Operation consisted of bilateral salpingo oophorectomy, appendectomy, and coagulation of cervix A graft, 14 by 6 centimeters, was applied to denuded terminal ileum Patient has remained cured to date

CASE 9 J G C, female aged 34 years, was operated upon on January 13, 1941 She had previously been operated upon, in 1933, at which time a right salpingo oophorectomy and appendectomy had been performed Examination revealed lower abdominal pain, excessive menstruation, habitual constipation since last operation A preoperative diagnosis of chronic pelvic inflammatory disease and chronic intestinal obstruction was made When the abdomen was opened a left chronic pyosalpingitis and oophor-

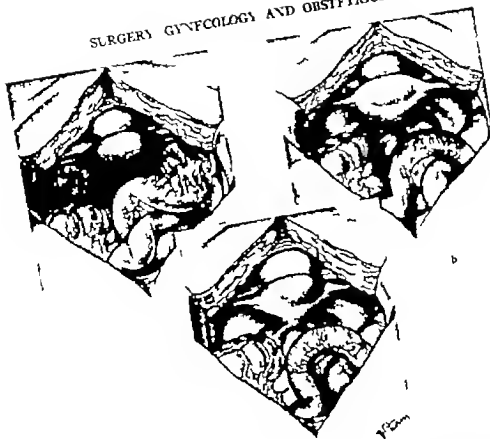


Fig. Case 3. a, Chronic bilateral tubo-ovarian mass. Terminal ileum densely adherent to right adnexal mass. b, Bilateral salpingo-oophorectomy. c, Free omental graft to terminal ileum.

III and pain throughout the lower abdomen of colic like nature which had been present for 6 days before admission to the hospital. No gas or feces had been passed for 7 hours. When the abdomen was opened thick layers of adhesions were noted throughout the right iliac fossa as well as chronic bilateral tubo-ovarian disease. The sigmoid was adherent to the uterus and left adnexal mass. The terminal ileum was densely adherent to the right adnexa. Bilateral salpingo-oophorectomy and supravaginal hysterectomy were done. Grafts were applied as follows: (1) 6 by 5 centimeter graft to cover denudation of left broad ligament and anterior sigmoid; (2) a 6 by 6 centimeter graft to cover denudation of terminal ileum; (3) a 6 by 5 centimeter graft to cover denudation of right broad ligament and anterior sigmoid. The patient gained in weight and had no gastrointestinal disturbances since discharge from hospital.

CASE 5. H. C. female aged 30 years, was operated upon 7 years ago. Bilateral salpingo-oophorectomy had been done in 1926. Patient complained of colic like pain vomiting and dilatation of abdomen. No feces had passed for 4 days, no gas for

24 hours. When the abdomen was opened the terminal ileum was found to be densely adherent to the right broad ligament posteriorly for 6 centimeters, kinked, and completely obstructed. Operation consisted of resection of the posterior wall of the right broad ligament. A graft, 8 by 5 centimeters, was anastomosed to the terminal ileum. Following operation bowel movements have been normal for first time in 4 years, and there has been no recurrence of the colic.

CASE 6. W. C. W. female aged 33 years, was operated upon April 23, 1926. Patient complained of alternating constipation and diarrhea. Peristalsis was visible in distention grade II. Scout film showed much gas in small intestine. The preoperative diagnosis was left ovary cyst, infected with chronic intestinal obstruction. When the abdomen was opened a large left cystic tubo-ovary mass was noted wedged into the pelvis minor; also right chronic salpingitis. At operation the left adnexal mass was excised and right salpingectomy performed.

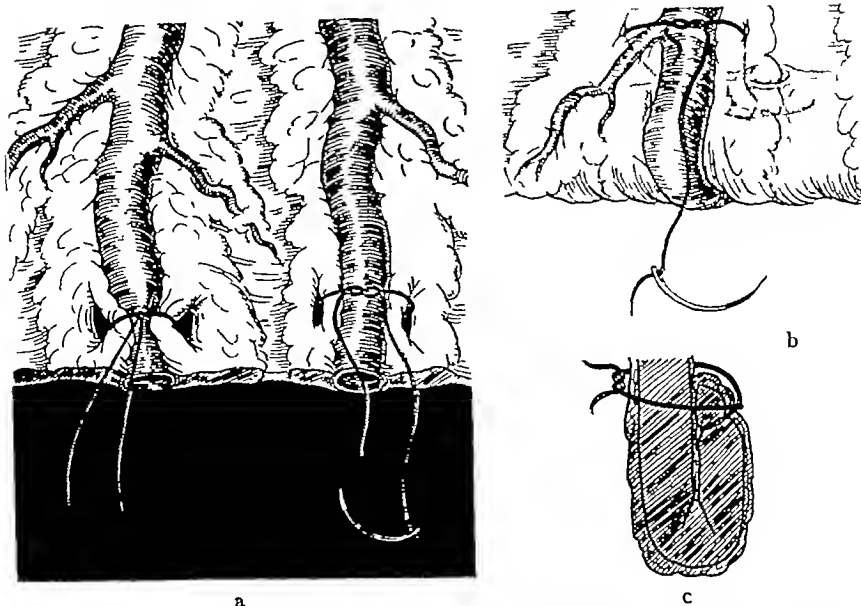


Fig 6 Technique of peritonealizing omental stumps and vessels a, First knot tied upon anterior or posterior leaf of intact omentum b, Ends of ligature rethreaded Edge rolled, then with blunt end of needle passed through omentum 1 to 2 centimeters above rolled edge, the second knot is tied c, Completely peritonealized omental stump

it and to the cecum. A total of approximately 20 centimeters of parts of the ileum was adherent to the uterus and left adnexa, hugging the uterus completely. The right adnexa were absent. Operation consisted of appendectomy, supravaginal hysterectomy, left salpingo oophorectomy and complete peritonealization of the pelvis. Grafts were applied as follows: (1) a 9 by 6 centimeter graft to the terminal ileum and cecum, (2) a 10 by 6 centimeter graft to one portion of the pelvic ileum, (3) a 6 by 6 centimeter graft to another portion of the pelvic ileum. Since operation, bowel movements are regular and there have been no gastrointestinal symptoms.

CASE 11 B R W, female, aged 26 years, secundipara, was operated upon June 8, 1941. Patient presented the textbook picture of chronic cholecystitis following marked digestive disturbances through both pregnancies, colic like attacks suggestive of stone. A cholecystogram was positive for cholecystitis but no stones were visible. A gastrointestinal series was positive for duodenal ulcer after complete atropinization. When the abdomen was opened there was revealed a strawberry gall bladder with thick percholecystic adhesions involving the gall bladder and entire anterior wall of the first portion of duodenum. There were no stones in gall bladder or ducts. Cholecystectomy was performed and first portion of duodenum was completely denuded. A graft 8 by 6 centimeters, was applied to the denuded duodenum. Since operation patient has had complete relief from digestive attacks and pain, is on regular diet, and has no distress after eating.

CASE 12 C B K, female, aged 26 years, was operated upon on August 3, 1941. She had previously had a cesarean section in 1939, and in 1940 adhesions between the small intestine and the uterine scar were broken up to relieve an acute intestinal obstruction. Examination revealed colic-like pain, vomiting.

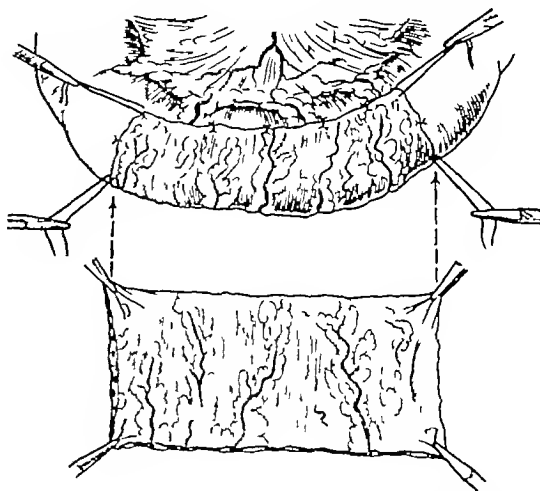


Fig 7 Omental graft as applied in dog experiments. Grafts measured 10 by 5 centimeters. Intestine completely encircled. Number 50, J & P Coats cotton sutures used, every 2 centimeters. Edges rolled under. Sutures clipped short.



Fig. 3. Scarified ileum. Dog 3. Photograph shows lack of excellent graft. Note ramifications of mesenteric vessels.

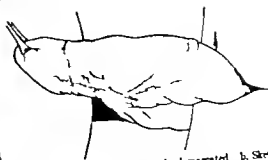


Fig. 4. Graft. This graft is sharply demarcated. Sketch showing mirror image of photograph.

intestine, were used as a base for the grafts.

In 5 dogs, free grafts 10 by 6 centimeters, were detached from the free border of the omentum. These grafts were attached without any injury to the intestine whatsoever (except for the needle punctures) to the entire circumference of the terminal ileum about 30 centimeters, from the ileocecal valve. For fixation, 50 cotton sutures were used approximately every 2 centimeters. In order to ensure future mesenteric blood supply the grafts were run on both sides, upon the mesenteric borders of the ileum. The edges were carefully tucked under and the sutures were clipped very short (Fig. 7).

In 5 more dogs, the surface of the terminal ileum, about 30 centimeters, from the ileocecal valve, was scarified over an area roughly 8 by 3 centimeters. Scarification was done with the cutting edge of a dull scalpel. Complete macroscopic denudation was easily accomplished. After the scarified surface was rubbed with a dry gauze sponge the graft was then applied as in the first series.

From 90 to 100 days after the application of the grafts, the dogs were relaparotomized. In Table I are tabulated the results of the experiments upon the unscarified intestine and in Table II are the results upon the scarified group.

In all of the dogs (5) where the grafts were laid upon the unharmed ileum (Table I) the omentum had completely wrapped itself around the segment operated upon in such a way that it was impossible to tell graft from enveloping omentum (Fig. 8 a and b). The only identifying remains of the grafts were the

cotton sutures used in securing the grafts in place. There were no other adhesions to intestines or to the omentum. The area of the omentum from which the free grafts had been excised had smoothed out completely though the ligatures were still loosely in place in several instances.

TABLE I.—FREE OMENTAL GRAFTS APPLIED TO UNSCARIFIED ILEUM (Relaparotomized after 3 months)

Dog 1	Normal omentum envelops grafted area throughout its length. Sutures, in place, glisten through omentum. No other adhesions.	
Dog 2	Graft enveloped as in Dog 1 completely. No adhesions.	Part of graft fixed
Dog 3	Same as Dog 1	
Dog 4	Same as Dog 1	
Dog 5	Same as Dog 1	

In 4 of the dogs in which the grafts had been applied to scarified intestine (Table II) the resulting patch was identified by the sutures still in place. The graft in all 4 dogs mentioned required careful inspection in order to outline it at all from normal ileum, so smooth and glistening was the surface (Figs. 9 a and b to a and b, 11 a and b, 12 a and b). The only irregularities consisted of blood vessels which had grown into the grafts from the mesentery and the remaining suture knots. Peristalsis continued normally through the grafts. Fine long white strands could be detected running veil like, through the length and breadth of the patch. They resembled strands of replacement fibrous connective tissue. Very little of the original fat of the graft remained. Roughly estimating it, not more than 25 per cent of the original fat in any of the grafts, remained after 3 months. The circumference and the diameter of the patched

THE RÔLE OF HYPERTENSION AND PANCREATIC EROSION IN MASSIVE FATAL HEMORRHAGE FROM GASTRIC AND DUODENAL ULCERS

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MANY factors influence the prognosis of massive hemorrhage from a gastric or duodenal ulcer. Among those most frequently mentioned in reports on this subject are (1) age, (2) number of hemorrhages, (3) arteriosclerosis (4) chronicity (5) sex, and (6) location.

The factors which are less frequently mentioned are (1) hypertension (2) erosion of the pancreaticoduodenal artery and (3) bleeding from granulation tissue buds in the base of the ulcer.

In a review of postmortem examinations of cases of fatal gastric and duodenal ulcer we were impressed by the high incidence of hypertension and pancreatic erosion in those patients who died of massive hemorrhage.

MATERIALS AND METHODS

In the Charity Hospital of Louisiana during the period from 1935-1941 the bodies of 81 patients who died as the result of gastric or duodenal ulcer were subjected to postmortem examination. Multiple ulcers were found in 11 cases, but only the ulcer which was responsible for the patient's death was used for the purpose of analysis.

The cases were divided into gastric and duodenal ulcer groups and in each group analyses were made concerning (1) the distribution of ulcers according to sex and color (2) the primary cause of death (3) the age range and average age of the patients at death, (4) the incidence of hypertension and (5) the incidence of pancreatic erosion.

The presence of hypertension was established by reviewing the clinic and hospital

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history records and the postmortem protocols. Because some patients were in a state of shock throughout their last hospital stay previous blood pressure readings taken when shock was not present, were reviewed on all cases.

Nineteen patients had hypertension. In 12, there was a diastolic blood pressure of 90 or more millimeters of mercury and a cardiac hypertrophy. Most of these patients also showed nephrosclerosis. In 5 the diagnosis of hypertension was based largely on the record of an elevated blood pressure. Four of these 5 patients showed diastolic blood pressures of 100 or more millimeters of mercury and one maintained a blood pressure of 130/76 millimeters of mercury in the presence of a gastric hemorrhage so severe that physical signs of shock and subjective symptoms of cerebral anemia were present. In 3 cases, cardiac hypertrophy alone formed the basis of the diagnosis. Causes of hypertrophy other than an elevated blood pressure were excluded.

Ten patients were classified as questionable cases of hypertension because the data obtained in the clinical and postmortem records, although suggestive of hypertension, were incomplete. These were counted as patients without hypertension in the calculation of percentages. The 52 remaining patients showed no clinical or postmortem evidence of hypertension.

With one exception (patient in shock with a blood pressure of 130/76 millimeters of mercury) the classification into the three groups was made without knowledge of the cause of death.

RESULTS

Distribution of gastric and duodenal ulcers according to sex and color. Forty-six, 56.7 per cent, of the 81 ulcers occurred in white patients

and 35, 43.2 per cent, occurred in negroes. Of the 46 ulcers found in white patients, 44 were found in males, and of the 35 ulcers found in colored patients, 31 occurred in males.

Thirty-three, 40.7 per cent, of the 81 ulcers were gastric and 48, 59.2 per cent, were duodenal. In white patients the ratio of duodenal to gastric ulcers was almost 2:1, whereas in negroes the ulcers occurred with almost equal frequency in the two sites.

Cause of death. Hemorrhage was the cause of death in 11 gastric and 8 duodenal ulcers, a total of 19 cases, 23.3 per cent. Perforation with ensuing localized or generalized inflammation in the peritoneal cavity caused death in 19 gastric and 36 duodenal ulcers, a total of 55 cases, 67.9 per cent. Miscellaneous causes accounted for death in 3 gastric and 4 duodenal ulcers, a total of 7 cases, 8.6 per cent. Among these cases there were 3 deaths from obstruction, 2 from operative procedures, and 1 each from bronchopneumonia and postoperative peritonitis.

Colored patients predominated in the group in which death was due to hemorrhage, and white patients in the group in which perforation was the cause of death.

Analysis of age. The average age of the colored patients in each group was less than that of the white patients in the corresponding group. The average age of patients who died of hemorrhage was 59.7 years, in those who died of perforation it was 50.1 years.

Relation of hypertension to cause of death. The incidence of hypertension in the entire group of 81 patients was 23.4 per cent. Of the 19 whose death was due to hemorrhage, 11, 57.8 per cent, had hypertension and of these 8 were colored and 3 were white. The incidence of hypertension among patients who bled fatally from gastric ulcers was essentially the same as the incidence among those who bled fatally from duodenal ulcers. Among the 55 patients whose death was due to perforation, 6, 11.1 per cent, had hypertension, and among the 7 patients whose death was due to miscellaneous causes, 2, 28.5 per cent, had hypertension.

Pancreatic erosion. In 7 patients the ulcer had eroded into the substance of the pancreas.

Hemorrhage was the primary cause of death in each instance. Two ulcers were located on the posterior surface of the pyloric portion of the stomach and 5 were located on the inferior surface of the first portion of the duodenum. All of these patients were males. Three patients in this group also had hypertension.

IMPORTANT FACTORS IN FATAL HEMORRHAGE

The predominance of duodenal ulcers over gastric ulcers, the average age of the patients in the hemorrhage group and the predominance of males over females is in accordance with the observations of many other investigators, even though 43.2 per cent of our patients were negroes. A finding which differs from that of other authors, however, is the presence of hypertension or erosion of the pancreas in 78.9 per cent of the hemorrhage cases.

In reports by other workers, hypertension has not received a prominent place among the factors which produce fatal hemorrhage. Jordan and Kiefer in 1932, in analyzing the factors which influence prognosis in the medical treatment of duodenal ulcer, noted that hypertension was present in 9 per cent of 53 patients in whom treatment was successful, whereas the incidence among 43 unsuccessfully treated patients was 33 per cent. In 12 of their patients treatment was considered to be unsuccessful because of hemorrhage. 4, 33 per cent, of these patients had hypertension. The authors did not relate the hemorrhage directly to the elevated blood pressure but stated that "the prognostic significance of hypertension appears to be related to the intolerance of alkalis." Pfeiffer and Meyer, Rosi, and Steigmann, in their reviews on bleeding ulcers, include hypertension as one of the factors which increases the mortality from hemorrhage, but they give no data to support their statements.

In our group, hypertension was associated with massive fatal hemorrhage in 57.8 per cent of the cases, as compared to an incidence of 23.4 per cent in the entire group and 11.1 per cent among the patients whose death was due to perforation. It should be emphasized that the actual incidence of hypertension in the hemorrhage group could not have been detected if only the blood pressure readings

taken during the final hospital stay had been considered. Only 5 of the 11 cases of hypertension in this group showed an elevated blood pressure during the time of their fatal hemorrhage. The clinic records, the records of previous hospital admissions, and the postmortem findings enabled us to establish the presence of hypertension in the 6 remaining cases.

The hospital record of 1 patient with massive gastric hemorrhage illustrates how blood pressure readings taken at the time of the hemorrhage may be misleading. The lowest reading taken during the time of the hemorrhage was normal 138/80 millimeters of mercury. A reading obtained one day prior to the severe hemorrhage was 180/106 millimeters of mercury and 5 days after the hemorrhage ceased the blood pressure was 144/110 millimeters of mercury. This patient was not included in the hemorrhage group because he subsequently died following a subtotal gastrectomy.

It is interesting to note that among the various factors which different investigators have found to be influential in the outcome of hemorrhage from gastric or duodenal ulcers there are several which are commonly associated with hypertension. It is commonly stated that fatal hemorrhage is more likely to occur in patients beyond the age of 50 or 55 years; the incidence of hypertension is higher in this age group. Arteriosclerosis is also mentioned as an important factor in fatal hemorrhage; vascular disease is common in patients with hypertension. The relatively high incidence of fatal hemorrhage in the colored as compared to the white race is probably correlated with the greater frequency of hypertension among negroes.

In our series, all 7 of the patients with erosion into the substance of the pancreas bled to death. We were not able to demonstrate the erosion of a large vessel such as the pancreaticoduodenal artery in any of these cases. It is probable that the action of digestive ferments on the walls of smaller blood vessels was largely responsible for these hemorrhages.

Our studies suggest that hypertension is an important factor in the causation of fatal hemorrhage from gastric and duodenal ulcers. We cannot be certain of the pathogenesis of the hemorrhage but it seems likely that injured vessels in the ulcer base may rupture more easily and bleed more profusely in the presence of an elevated, than in the presence of a normal blood pressure. The accepted explanation of spontaneous cerebral hemorrhage in patients with hypertension is based upon this same principle.

SUMMARY

1. Nineteen, 23.3 per cent, of 81 patients with gastric or duodenal ulcer died of hemorrhage as shown by postmortem examination.
2. Eleven, 57.8 per cent of these 19 patients had hypertension.
3. Four of these 19 patients had erosion of the pancreas without hypertension and 3 had both hypertension and pancreatic erosion.
4. Fifteen, 78.9 per cent of the 19 patients had either hypertension or erosion of the pancreas, or both.

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SIGNIFICANCE OF CHANGES IN SUBDIVISIONS OF THE LUNG VOLUME IN THE TRENDELENBURG POSITION

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COMPARISONS of the volumes of the various subdivisions of the total lung volume in patients in the sitting and in the recumbent position have been made by several authors (1, 3, 7, 9, 11, 14), their findings have been analyzed by McMichael and McGibbon. No data are available, however, on the changes which occur when the patient assumes the Trendelenburg position. Since this position is employed routinely in certain surgical operations and with great frequency in the treatment of shock and peripheral vascular disease, it appeared desirable to study the effect of the head-down position on pulmonary volume and dynamics.

Studies were made 1 to 3 hours after the last meal on 6 normal subjects, 3 male (subjects 1, 2, 3) and 3 female (subjects 4, 5, 6), aged 20 to 35 years. A tilting table was used in these experiments. All the measurements were made 15 to 20 minutes after a given position was assumed. Measurements of the subdivisions of the pulmonary volume were first made with the subject flat, after which the table was tilted so that the subject's body, with head down, made an angle of 22.5 degrees with the horizontal. Following this, studies were made with the subject in the head-up position at an angle of 25 degrees with the horizontal. Two to 8 measurements were made in each position. Estimations of tidal air, respiratory minute volume, and oxygen consumption were also made. The method of Christie (4), slightly modified as described previously (10), was used in these studies.

RESULTS OF STUDY

The *functional residual air* was uniformly smallest with subject in the head-down position, intermediate with subject in the flat position, and largest with subject in the head-

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up position. The functional residual air ranged between 280 and 500 cubic centimeters, or between 9.5 and 23.8 per cent less with subject in the head-down position than in the flat position, the average difference was 363 cubic centimeters, or 17.2 per cent.

The *reserve air*, one of the two components of the functional residual air, was uniformly smallest with patient in the head-down, intermediate in the flat, and largest in the head-up positions. The reserve air with subject in the head-down position varied from 185 to 360 cubic centimeters, or from 19.4 to 51.9 per cent less than that in flat position, average difference, 253 cubic centimeters, 39.8 per cent.

The variation in the volume of the other component of the functional residual air, the *residual air*, with subjects in the three positions was no greater than the variation in successive measurements made with patient in any one position. The residual air in patients in the head-down position ranged between 20 and 165 cubic centimeters, or between 1.0 and 14.6 per cent less than that in the flat position, the average difference was 100 cubic centimeters, or 7.3 per cent.

The *complemental air* in 5 instances was greater with subjects in the head-down than in the flat position, in the sixth subject this relationship was reversed, but the difference between the two values was only 35 cubic centimeters. The complemental air was uniformly lowest with subject in the head-up position. The values in the head-down position were between 35 cubic centimeters less and 200 cubic centimeters greater than the values in the flat position, or minus 1.2 to plus 5.7 per cent of the latter value, average difference, 93 cubic centimeters, 2.9 per cent.

The *vital capacity* was uniformly smaller with patients in the head-down position than in the head-up position. However, it was intermediate in only 4 of the 6 subjects in the

TABLE L—RESPIRATORY DYNAMICS AND SUBDIVISIONS OF TOTAL LUNG VOLUME IN VARIOUS POSITIONS

Case	Resp. rate per min.	Tidal vol. c.	Resp. vol. l./min.	O ₂ consumption c./min.	Functional residual vol. c.	Residual R.V. c.	Reserve vol. c.	Complemental vol. c.	Vital capacity c.c.	Total capacity c.	Head Position
		485	37	128	1490	1030	540	1490	4005	4925	Flat
		485	37	125	1390	1030	460	1370	3830	4780	Head down 5°
9	335	125	255	1740	1900	1300	600	1300	4175	4630	Head up 15°
10	335	125	255	1740	1900	1300	600	1300	4175	4630	Flat
11	335	125	255	1740	1900	1300	600	1300	4175	4630	Head down 5°
12	335	125	255	1740	1900	1300	600	1300	4175	4630	Head up 15°
13	335	125	255	1740	1900	1300	600	1300	4175	4630	Flat
14	335	125	255	1740	1900	1300	600	1300	4175	4630	Head down 15°
15	335	125	255	1740	1900	1300	600	1300	4175	4630	Head up 15°
16	335	125	255	1740	1900	1300	600	1300	4175	4630	Flat
17	335	125	255	1740	1900	1300	600	1300	4175	4630	Head down 15°
18	335	125	255	1740	1900	1300	600	1300	4175	4630	Head up 15°
19	335	125	255	1740	1900	1300	600	1300	4175	4630	Flat
20	335	125	255	1740	1900	1300	600	1300	4175	4630	Head down 15°
21	335	125	255	1740	1900	1300	600	1300	4175	4630	Head up 15°
22	335	125	255	1740	1900	1300	600	1300	4175	4630	Flat
23	335	125	255	1740	1900	1300	600	1300	4175	4630	Head down 15°
24	335	125	255	1740	1900	1300	600	1300	4175	4630	Head up 15°
25	335	125	255	1740	1900	1300	600	1300	4175	4630	Flat
26	335	125	255	1740	1900	1300	600	1300	4175	4630	Head down 15°
27	335	125	255	1740	1900	1300	600	1300	4175	4630	Head up 15°
28	335	125	255	1740	1900	1300	600	1300	4175	4630	Flat
29	335	125	255	1740	1900	1300	600	1300	4175	4630	Head down 15°
30	335	125	255	1740	1900	1300	600	1300	4175	4630	Head up 15°

flat position, being identical in the 3 others with the vital capacity in the head-down or the head-up position. The vital capacity in the head-down position was from 0 to 395 cubic centimeters, or from 0 to 10.3 per cent less than the vital capacity in the flat position the average difference was 164 cubic centimeters, or 4.6 per cent. The greatest difference between the head up and the head down positions was observed in the subject in whom the complemental air was not increased in the head-down position. The tidal air respiratory rate respiratory minute volume and oxygen consumption showed no constant changes in the various positions studied.

EVALUATION OF STUDY

The changes in the various subdivisions of the pulmonary volume in the Trendelenburg position are due entirely to variations in the volume of the reserve and complemental airs, since the residual air is essentially unchanged. Other authors have observed a decrease in the reserve air and an increase in the complemental air in the recumbent as compared

to the sitting position (1, 9, 11, 14). McMichael and McGibbon have demonstrated that these changes are due to the cephalad shift of the diaphragm which occurs in recumbency. It appears therefore that the further decrease in reserve and increase in complemental air in the Trendelenburg position result from a more marked cephalad diaphragmatic shift. This is apparently due to the pressure of the abdominal viscera on the diaphragm.

The complemental air increases less than the reserve air decreases in changing from the head-up to the flat and then to the head-down position. Accordingly the vital capacity and total pulmonary volume decrease slightly. This has been ascribed to an increase in the amount of blood in the lungs (11) but the evidence in this regard is not conclusive. Certainly these changes are too small to be considered significant. It is to be noted that the insignificant decreases in vital and total capacities fail to reveal the important changes in pulmonary dynamics which result from the head-down position. These are revealed only by consideration of the variations in the func-

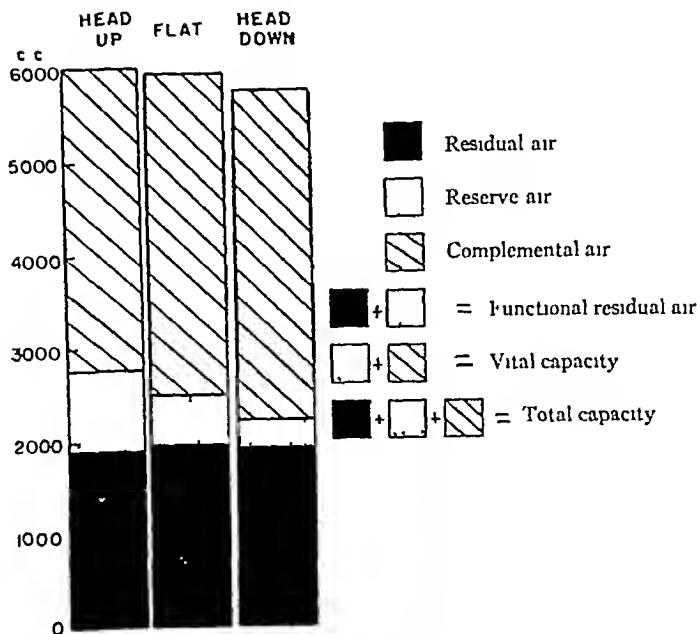


Fig 1 Changes in the lung volume and its subdivisions in various positions

tional residual air Changes in functional residual air are significant because they may be correlated with changes in the intrapleural pressure Christie and McIntosh (5) observed a decrease in the volume of the functional residual air of 230 to 440 cubic centimeters accompanied by a decrease in the negativity of the intrapleural pressure of 2.0 to 3.2 centimeters of water in the flat, as compared to the sitting position In the present study a further diminution in the volume of the functional residual air of almost the same magnitude occurred in patients in the head-down, as compared to the flat, position, presumably this change was accompanied by a still further decrease in the negativity of the intrapleural pressure of 2.0 to 3.0 centimeters of water Decrease in the volume of the functional residual air indicates a state of partial collapse of the lungs, with a reduction in respiratory space averaging approximately 20 per cent, this interferes with the aeration of blood flowing through the lungs A further impediment to respiration in patients in the head-down position is related to the necessity for moving the weight of the abdominal viscera upward during inspiration Judging by the

sensations experienced by the subjects of the present study in the head-down position, the interference with respiration is not important in normal individuals However, in the case of patients in shock or under the influence of depressing sedatives, it might be appreciable Shallow respiration and cyanosis are frequently noted in patients in whom paralysis of the lower intercostal muscles has occurred as a result of spinal anesthesia and it is not unlikely that this respiratory embarrassment is due in part at least to the changes in the lungs resulting from the Trendelenburg position frequently used in patients receiving this type of anesthesia It has been noted by anesthetists that patients operated upon in an extreme Trendelenburg position may breathe inadequately and become cyanotic, this is relieved by restoring the position of the patient to, or toward, the horizontal

Diminution in the negativity of the intrapleural pressure interferes with the return of blood to the heart and should give rise to an increase in peripheral but not in intrathoracic venous pressure Significant increases in antecubital venous pressure have been described in the head-down position by Henderson and

Haggard, Asmussen et al and Schott and Spatz. If this elevation of venous pressure were present also in the great veins within the thorax, an increase in cardiac output should occur in patients in the head-down position. However Asmussen et al found no change in the cardiac output in patients in the head down position, and Donal et al reported a decrease of 23 per cent in subjects in this position. The finding of a marked decrease in pulse rate (2-8) beginning immediately on the subject's assuming the head-down position, further suggests that a fall in venous return occurs. It is doubtful whether the slightly decreased venous return in subjects in the Trendelenburg position exerts any deleterious effect in normal man. In patients in shock, however when the venous return is already diminished it would appear that further interference with the return of blood to the heart resulting from the Trendelenburg position may be definitely harmful.

It has been assumed that the Trendelenburg position causes the drainage of significant amounts of blood from the lower part of the body and also favorably influences circulation through the brain. Data bearing on the former were reported by Asmussen et al. who showed that only 100 cubic centimeters of blood are drained from the legs after the head-down position at an angle of 22.5 degrees is assumed. Similarly it is unlikely that the circulation through the brain is increased in subjects in the head-down position, since the cerebrospinal fluid pressure within the cranium is increased, and it has been shown in animals that this results in a brief slowing of the circulation followed by a return to normal (15).

It appears therefore that the Trendelenburg position obtains no advantages for the circulation of the brain over the flat position and may well be less favorable so far as respiration and circulation are concerned. In patients in shock or under the influence of sedatives or spinal anesthesia, it may be harmful.

SUMMARY AND CONCLUSIONS

1. Measurements of the subdivisions of the total lung volume and of the pulmonary dy-

namics were made in 6 normal subjects in the Trendelenburg, flat and head-up positions.

2. The residual air was unchanged in the various positions studied, and the vital and total capacities varied only slightly. The vital and total capacities were lowest in the Trendelenburg. Intermediate in the flat, and greatest in the head-up positions.

3. Striking changes in reserve and complementary air volumes occurred. The reserve air was lowest in Trendelenburg and greatest in head-up positions; the complementary air varied inversely with reserve air. These changes were interpreted as due to a cephalad shift of diaphragm in patients in head-down position.

4. The changes in the functional residual air are significant in that they afford information on changes in the intrapleural pressure. Decrease of the functional residual air in the Trendelenburg position suggests that changes in intrapleural pressure occur in this position which tend to make respiration more difficult and impair return of venous blood to heart.

5. No consistent changes in respiratory dynamics were observed in the various positions studied.

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STONE IN THE URETER

Clinical Data Based on 500 Cases

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THIS paper is based on a study of 500 unselected patients with stone in the ureter, covering a period from 1917 to 1941. The 500 unselected cases do not represent all the patients seen, but I believe the number is large enough for purposes of study, since, being unselected, they are fairly representative of the cases seen in the average urologic practice.

Sex. The question of sex is of little aid in the diagnosis. It is the general consensus that this condition occurs much more frequently in men than in women, and my experience is in keeping with this general point of view, since of the 500 patients studied 400 were males and only 100 were females.

Age. It is a well known fact that stone in the ureter is rare at the extremes of life. The youngest patient in this series was 2 years old and the oldest, 80. Stone occurred with the greatest frequency in the third, fourth, and fifth decades. This is in keeping with experiences in general. The age incidence in our group was as follows: 2 patients in the first decade of life, 9 in the second, 74 in the third, 131 in the fourth, 137 in the fifth, 82 in the sixth, 32 in the seventh, 9 in the eighth, 1 in the ninth, and 23 patients whose ages were not stated.

Location. So far as being an aid in the diagnosis, the question of whether stone occurs more frequently on the right or left side is of little moment, except when the stone occurs on the right side it is frequently confused with appendicitis. There was not much variation in the two sides in my series, as the stone was located on the right side in 229, or 45.8 per cent of my patients, on the left side in 259, 51.8 per cent, and on both sides in 12, or 2.4 per cent of my patients.

THE STONE

Number of stones. In the largest number of instances the symptoms are due to the presence of a single stone. In this series, 447, or 89.4 per cent, of the patients had a single stone, and only 53, or 10.6 per cent, had multiple stones. Nevertheless, the question as to whether the patient is suffering from multiple stones is of importance as regards prognosis and management, and will be considered under treatment. I always make it a point to call the patient's attention to the fact that multiple stones are present. Unless this is done, the patient may be less vigilant as regards a search for the passage of the second stone.

Multiple stones may vary greatly in number from 2 to 100 or more. In one instance, a patient, who was a physician, passed 28 stones after a very severe attack of colic. In another instance the ureter harbored stones from the vesical end to the fourth lumbar vertebra (Fig. 1). Multiple stones, in one patient, were left behind after a nephrectomy which was performed elsewhere. Because of grave symptoms it was necessary to perform a ureterectomy (Fig. 2).

Size. Fortunately, most stones in the ureter are small. They may vary in size from a grain of wheat to a stone of enormous size and weight (5). The size has a direct bearing on prognosis and treatment (Fig. 3). This will be discussed under these headings.

Chemical composition of stones.¹ The results of chemical examinations of stones are available in 102 patients. This number is deemed sufficient to serve as a cross index of the chemical composition of the stones in this series. One is impressed by the fact that in only 9 cases, only 1 element was present. Analyses in the 102 cases are given in Tables I and II.

Read before the Western Surgical Association, St. Paul, Minnesota, December 6, 1941.

¹The chemical analyses were made by Dr. M. R. Freeland, chemist to the Presbyterian Hospital.

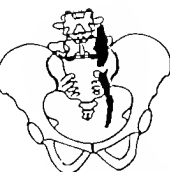


Fig. 2

Multiple stones in the left ureter
Fig. 3 A very large stone in the right ureter

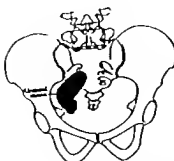


Fig. 3

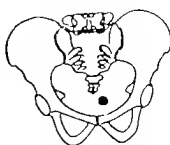


Fig. 4

Showing the presence of calculus in ureter. Because of the shape and location it is confused with bladder calculus

SYMPTOMS AND SIGNS

Pain. Pain may be either the first symptom or it may occur during the course of the disease. Pain was the first symptom for which relief was sought in 440 cases or 88.0 per cent. But the onset of the illness is not always

ushered in with pain since a number of patients have other initiating symptoms. For instance when a stone becomes engaged in the intramural part of the ureter or when it forms in a cystic dilatation of the ureter the onset of symptoms may be vesical in character (Fig. 4). Besides the presence of initiating pain pain occurring at some time during the illness was recorded in 468 patients, or 93.6 per cent.

The character of the pain is generally typical for stone, although there are exceptions. But not always does the pain radiate downward along the course of the ureter to the internal or external genitalia nor upward into the renal area.

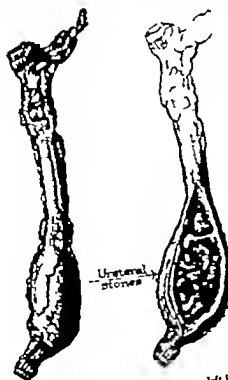


Fig. 5 Ureterectomy for calculi that are left in ureter following nephrectomy performed elsewhere

TABLE 1—PURE STONES—OXE ELEMENT ONLY FOUND

Case No.	Sex	Initials	Element per cent
31	M	K S	Calcium oxalate
34	M	K S	Calcium oxalate
37	F	M W	Calcium oxalate
38	M	G	Calcium oxalate
39	F	M H	Uric acid
40	F	B	Calcium phosphate
41	M	M	Calcium phosphate
42	M	W H B	Cystine
43	M	T	Triple phosphate

TABLE II.—CASES WITH STONES OF MORE THAN ONE ELEMENT—Continued

Case No. Sex	Initial	Predominant element	Other elements present								
			Calcium			Lanthanum oxide	Triple Phosphate	Oxal- acid	Fibrous	Magnesian amorphous phosphate	Papillary
			Phosphate	Oxalate	Carbonate						
7	B K	Calcium phosphate		+				+			
8	W B S	Calcium phosphate		+				+			
11	H P	Calcium phosphate		+				+			
12	A H	Calcium phosphate		+	+			+			
13	J C	Calcium phosphate		+				Trace			
14	W O McJ	Calcium phosphate		+		Trace					
15	W B D	Calcium phosphate		+				Trace			
16	E S	Calcium phosphate		+		+					
17	D L	Calcium phosphate		+	+	+					
18	S	Calcium phosphate		+				Trace			
19	B J S	Calcium phosphate		+				Trace			
20	C S	Calcium phosphate		+							
21	F W S	Calcium phosphate		+							
22	L C	Calcium phosphate		+							
23	J T M	Calcium phosphate		+				Trace			
24	M	Calcium phosphate		+							
25	W B V	Calcium phosphate		+				Trace			
26	J M	Calcium oxalate	+				+		Latic		
27	L S	Calcium oxalate	+								
28	K	Calcium oxalate	+					+			
29	A C	Calcium oxalate	+								
30	E G N	Calcium oxalate	+					+			
31	I B	Calcium oxalate	+					Trace			
32	J C McJ	Calcium oxalate	+					+			
33	C O	Calcium oxalate	+		+			Trace			
34	F A	Calcium oxalate	+								
35	L P	Calcium oxalate	+		+	+					
36	G	Calcium oxalate	+								

TABLE II—CASES WITH STONES OF MORE THAN ONE ELEMENT—Continued

TABLE II.—CASES WITH STONES			Other element present								
Case No. Sex	Initials	Predominant element	Calcium			Ammonium urate	Triple Phosphate	Uric Acid	Fibrous	Magnesium ammonium phosphate	Miscellaneous
			Phosphate	Oxalate	Carbonate						
✓	P B	Calcium carbonate	+	+		+					
46	A H	Calcium carbonate	+	+		Trace					
47	R	Triple phosphate			+	+					
48	C J D	Triple phosphate		Trace		Trace					
49	F	Triple phosphate		+					Trace		Crystals
50	B	Cystine									
51	M B	C " "	+	+							
52	J R	Magnesium ammonium phosphate			+	+					
53	C	Magnesium ammonium phosphate			+				Trace		

SUMMARY

Case

SUMMARY

Cases

48

 Cystine predominant
 Magnesium ammonium phosphate predominant
 Total cases

Cases

100

 One element only present
 Calcium phosphate predominant
 Calcium oxalate predominant
 Calcium carbonate predominant
 Triple phosphate predominant

The severity of the pain deserves careful analysis. The question which should arise is: Was the attack relieved by simple measures or was it necessary to resort to a hypodermic of morphine? A sudden onset of severe abdominal pain requiring morphine for relief should at once suggest either urinary or biliary stone colic. Not to weaken this statement thought should be given to the fact that the tablets may have equal severe pain.

Hematuria. Hematuria may be the first and only symptom of which the patient complains. Furthermore, it should be remembered that stone is one of the five common causes for blood in the urine. In practically all the patients in this series the hematuria was followed by pain. But not infrequently hematuria and pain occur simultaneously. Hematuria was present in 81 patients or 34.2 per cent at some time during the illness and it was present in 23 patients, or 4.6 per cent as the first symptom noted by the patient. Every patient routinely is specifically asked whether he or she has ever noticed blood in the urine.

Nausea and vomiting. Reflex nausea and vomiting occur with renal and ureteral stone colic. Some of the patients in this series complained of nausea alone but, on the other hand, both nausea and vomiting occurred in 231 patients, or 46.2 per cent.

Previous passage of stones. The history of a previous passage of stones is most important and one must never fail to ask the patient the specific question as to whether sand, gravel, or stone has been previously passed. Naturally, if a patient gives a history of having passed stones on one or more occasions, the odds are in favor of passing stones again, hence the benefit of watchful waiting should be the order of the day before cystoscopic manipulation or advancing operation. Because of the importance in prognosis as well as in outlining treatment, I make it a rule to ask this specific question of each patient. Seventy-one patients, 14.2 per cent in this series, gave a history of having passed stones previously, therefore observation and study were of prime importance before instituting treatment.

Other symptoms Backache, so common in lesions of the urinary organs, was present in 186 patients, or 37.2 per cent. Frequency of urination was present in 42 per cent, and burning in 30.4 per cent. One hundred eighty patients, or 36 per cent, stated that pus had been previously found in the urine either by physicians or by laboratory bureaus, to which they were subscribers, advising that they should consult their family physicians. This is a relatively high percentage, and a significant one as far as the patient is concerned. Chills and fever were present in 88 patients, or 17.6 per cent.

In Table III are recorded the symptoms which occurred most frequently

TABLE III

	No. patients	Per cent
Pain	468	93.6
Hematuria	171	34.2
Nausea and vomiting	231	46.2
Frequency	211	42
Pyuria	180	36
Backache	186	37.2
Burning	152	30.4
Chills and fever	88	17.6
Passage of stones	71	14.2

THE EXAMINATION

Urinalysis Next in importance to the history and physical examination is the urinalysis. If we bear in mind the ease with which this examination can be carried out and the invaluable information it gives, one cannot help but stress its importance, especially when coupled with the history. As previously stated, many patients were seen because of the fact that pathological elements were found in the urine. It should be emphasized here that one negative report is not indicative that pathology is nonexistent. The number of positive findings were truly amazing, since a study of the patients in this series revealed that the findings were positive in 393 patients and negative in only 78. In 29 patients no data were available. In other words, the findings were positive in 83.43 per cent and negative in 15.56 per cent. In some of the patients of the group more than one pathological element was found.

The results of the urinary examination were as follows: albumin in 122 patients, or 24.4 per cent, sugar in 4 patients, or .8 per cent, red

blood cells in 215 patients, or 43 per cent, white blood cells in 346 patients, or 69.2 per cent, casts in 38 patients, or 7.6 per cent.

In a case of suspected stone one should never be satisfied with the results of a single examination, especially if it is negative, which occurs not at all infrequently when the stone produces a temporary block on the affected side, hence the importance of repeated examinations cannot be overemphasized. Examination of a number of specimens pertaining to the same patient may yield only negative results, when unexpectedly the next examination will show many fresh red blood cells, pus cells, or both.

Culture studies of the urine Cultures, unfortunately, were not obtained in each case due to the fact that some of the patients were seen before bacteriological studies of the urine were a matter of routine, a procedure now followed to the letter. However, cultures were made in 385 patients of which 133 were positive, an incidence of 34.54 per cent, and 252, or 65.43 per cent, were sterile.

Blood pressure studies In this study, blood pressure findings were normal except in patients in the older age group—a group at a time of life when an increase in blood pressure is not uncommon—and were not considered of special significance so far as the diagnosis or treatment was concerned.

Roentgen-ray observations With the results of a careful history and physical examination coupled with the urinary findings, strong, presumptive evidence of stone is at hand. The next logical procedure is the roentgen-ray examination which begins with a plain film, or set of films, that includes the entire urinary tract. The two essentials are films of good quality and the correct interpretation of the shadows shown.

Of these two essentials, quality of the films at the present time is above reproach. But, on the other hand, correct reading and proper interpretation are most important. I am sure that everyone has had the experience of receiving a negative report only to have the patient pass a stone a few days later, which, in the light of events, leads to a review of the films with the result that a previously overlooked shadow is seen that corresponds in shape and

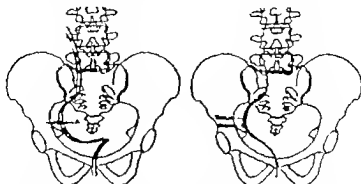


Fig. 5, left: Showing the shadow in apparent contact with the shadow graph catheter after the shift to the x-ray tube. (See Fig. 6.)

Fig. 6. Retrograde pyelogram showing the shadow outside the ureter.

size to the stone brought in by the patient and is absent in subsequent films. The importance of careful film reading cannot be overemphasized.

In some of the patients in whom the roentgenogram failed to demonstrate the stone shadow the cystoscopic examination disclosed the stone in or protruding from the ureteral orifice. In others the orifice was edematous and swollen clearly indicating a pathological

condition. In others still the mucosa was red due to the presence of blood which, in turn, was the result of trauma inflicted by the stone in its passage.

Peterson and Holmes, in a study of 100 roentgen reports of patients suspected of having ureteral stones found that 21 films gave no indication of any shadows which might be interpreted as calculi. These films were then carefully restudied abetted by the clinical data in each case and shadows, which as questionably represented the calculi, were seen in 1 of the 21 cases.

A study of the roentgen findings in this series disclosed that positive reports for stone were recorded in 455 patients, while the reports were negative in only 20 patients. Twenty-three passed their stones before or during the time they were under my observation and in 2 patients the roentgen reports were missing. A review of these cases therefore reveals positive roentgen reports in 95.79 per cent and negative reports in 4.21 per cent.

The presence of a shadow along the course of the ureter warrants further investigation to determine whether one is dealing with a stone or with an extraureteral shadow (Figs. 5-6). This can be done by the use of a shadowgraph catheter with a double exposure film and shift in the tube a procedure previously described (6).

In the case of very stout patients the films may not be clear and the shadow under study may be lost. Because of this possibility it is advantageous to use two films, a point which

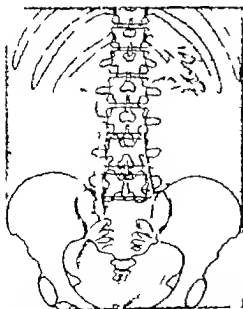


Fig. 7. Showing the presence of shadow in the region of the right kidney. Such are confused with calculi; they were due to enteric coated pills of ammonium chloride.

was recently mentioned by Peterson and Holmes

Possible sources of error in this procedure (shadowgraph catheter) are the presence of a stone in a diverticulum of the ureter or a stone in a double ureter, only one of which has been catheterized

Confusion with extraureteral shadow-producing bodies has been discussed so often that I shall refrain from doing so here. I wish only to call attention to a new factor that may lead to confusion in diagnosis—namely, the presence of shadows produced by enteric coated pills. I know of one instance in which a patient was recently operated on for stone, when the shadow was actually due to an enteric coated pill. Because of the prevalent use of these pills, this possibility must always be borne in mind. To substantiate the truth of this statement, only recently a patient was sent in with the diagnosis of multiple kidney stones, the shadows having been caused by enteric coated pills (Fig 7)

Intravenous urography. The intravenous urogram is of much aid. In the largest number of instances it reveals dilatation of the ureter and of the kidney pelvis. Stone in the ureter is probably the most frequent cause of hydronephrosis. Although dilatation (except when the stones are very small) is the rule, I have seen a number of patients in whom the urograms disclosed no dilatation, despite the fact that the stones were far from small. The urogram not infrequently reveals the ureter down to the bladder or the outline may stop at the site of the stone, disclosing a complete block. This should cause no undue alarm, since the block, as the stone changes its position, is relieved.

In some instances the urogram fails to visualize the outline of the pelvis and ureter. When this occurs an increased density of the kidney outline is shown, therefore the kidney is more definitely outlined than its mate on the opposite side. The density is probably due to a temporary inhibition of function. I have seen this in several patients who were advised to have an immediate operation in one instance a nephrectomy. Subsequent study after the passage of the stone disclosed a complete return of function. Likewise in patients

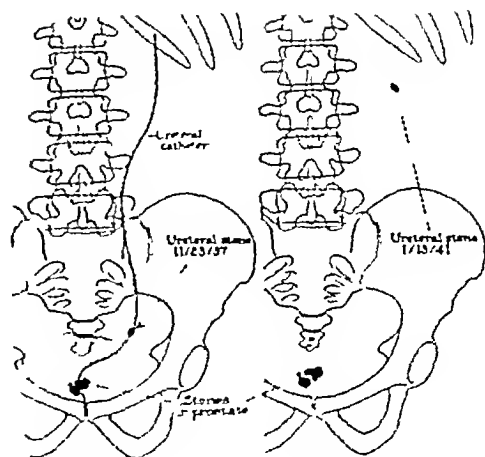


Fig 8 Retrograde movement of ureteral calculus

studied after stones were passed, the dilatation of the ureter and kidney pelvis disappeared except of course in those patients in whom some other pathological condition was present.

Retrograde movement of stone. In a previous publication (7) I called attention to the possibility of retrograde movement, which was not generally recognized at that time, and reviewed the cases in the literature. Because of this possibility a roentgenogram should be made on each patient just before operation, thereby avoiding the embarrassment of operating only to find that the stone had wandered up the ureter or into the kidney pelvis (Fig 8). This phenomenon occurs in children (8) as well as in adults and more frequently than is generally appreciated. Retrograde movement of the stone occurred in 10 patients in the present series.

A review of these 500 case histories reveals that 442 are available for study. The 58 remaining cannot be used because some of the patients were seen but once, others refused to follow advice, some discontinued treatment, and others still could not be located to determine the ultimate result of treatment. The results are recorded as follows: stones passed without instrumentation in 128 patients, or 28.9 percent; stones passed with instrumentation in 106 patients, or 24.1 percent; stones removed by operation in 112 patients, or 25.7 percent; still under observation and treat-

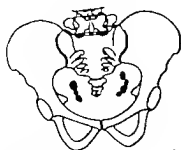


Fig. Bilateral multiple ureteral calculi. They are passed spontaneously

ment in 4 patients, or 9 per cent (3 patients are under observation because the stone had wandered back into the kidney but caused no symptoms 2 patients are under treatment)

TREATMENT

The treatment of stone in the ureter naturally falls into three groups: watchful waiting, instrumental manipulation, operative treatment.

Watchful waiting. It is to be borne in mind that many of these patients pass their stones without the use of instruments by the simple expedient of drinking large quantities of fluids, with or without the administration of diuretic drugs.

A careful history will reveal the fact that a significant number of these patients have previously passed stones, sometimes an indeterminate number of years ago and not seldom more or less recently. This has been the case in this series since the records show 14.3 per cent under the head of patients who have passed stones before coming under observation. It goes without saying that instrumentation in these patients is to put it mildly superfluous.

The statement of a patient that attacks of renal colic were followed by the passage of stones, should not go unheeded, and justifies a period of "watchful waiting." To subject a patient to cystoscopic manipulation just because of an attack of renal colic, unless immediate relief of obstruction is indicated, is not only unnecessary but condemnatory. Because a stone does not move a certain amount each day does not, in my opinion, justify manipulation. I have seen patients in whom no movement of a stone occurred for weeks or

months without any untoward symptoms, to be followed by the passing of the stone without medical aid just when my advice was forthcoming that an operation was necessary (Fig. 9).

In this series there were 128 patients or 28.9 per cent, who passed stones without manipulation of any sort.

Instrumental manipulation. It might be well to emphasize the fact that manipulation of a stone with instruments is not entirely free from danger and this phase has recently received attention in the literature (Wesson, Stevens, Lynch and Thompson, Woodruff, Henline, and others). Rusche and Bacon have emphasized the fact that the incidence of ureteral injuries has increased since the advent of a multiplicity of instruments designed to aid the passage of or to extract the ureteral stone. They report a series of 16 patients who suffered from injury to the ureter due to cystoscopic intraureteral instrumentation. Interestingly, too, is the fact that in the discussion of papers dealing with the danger of injury individual experiences are related by the discussants, which lead one to the inevitable conclusion that injury is far more frequent than one suspects.

I should like to state here that in this series there is no record of injury to the ureter in a single patient.

What injuries may occur from the use of the various types of stone extractors seems reasonable enough when we consider that their use depends mostly upon force and less upon dilatation. The stone if left to its own machinations dilates the ureter in its progress downward, a similar process being found in the realm of obstetrics. It seems to me that dilatation as a factor is most important and, while it is not without triumph to remove the stone at the first treatment, nevertheless it is advisable to exercise a considerable degree of caution when this type of procedure is undertaken.

Apprehensive of the danger of injury I made it a point to rely on simple dilatation and to inject sterile oil in practically all the patients in this series. Some of the various "stone extractors" were used in a few patients mindful always of the possible injury to the

ureter, a possibility fraught with danger that has militated against their use. While the dilatation and injection of oil is slower and requires more manipulations than the extractive methods, in my opinion the former procedure is decidedly less dangerous to the patient.

The patient, as well as the physician, it should be stated here, is desirous of a cure to be effected as soon as possible, and this brings up the question of how frequently manipulation should be resorted to. There is danger in manipulations that are too frequently repeated. The possible trauma produced by one treatment should be completely healed before the next manipulation is carried out. That ureteral catheterization may cause traumatism is evidenced by the fact that in simple cases, bloody urine occasionally occurs, or a small clot may be seen hanging from the ureteral orifice at a subsequent cystoscopic examination. These patients should not be subjected to manipulation again until the effects of trauma resulting from the previous instrumentation are no longer evident. If one adds to this picture the additional trauma produced by impacted stones, plus local inflammatory changes in the ureter around the stone, the danger of injury is not a remote possibility. It is for these reasons that I have always taken the position that manipulations should not be carried out too frequently and that they should be effected with a minimum of force so as to prevent trauma.

The treatment of stone by manipulation deserves careful consideration in each case. Not seldom, but, I regret to state, too often, the advice given is embarrassing, to say the least, since many of us have had the experience of treating a relatively large stone by manipulation without beneficial results, and then urging the patient to be operated on, advancing all the arguments in favor of an operation and stating the reasons why further use of instruments would be of no avail, only to have the patient pass the stone without further local treatment. The use of instrumentation for a small stone is, in my opinion, never justified, if the stone progresses down the ureter with each attack of pain, and especially if the patient, as mentioned, has previously passed stones.

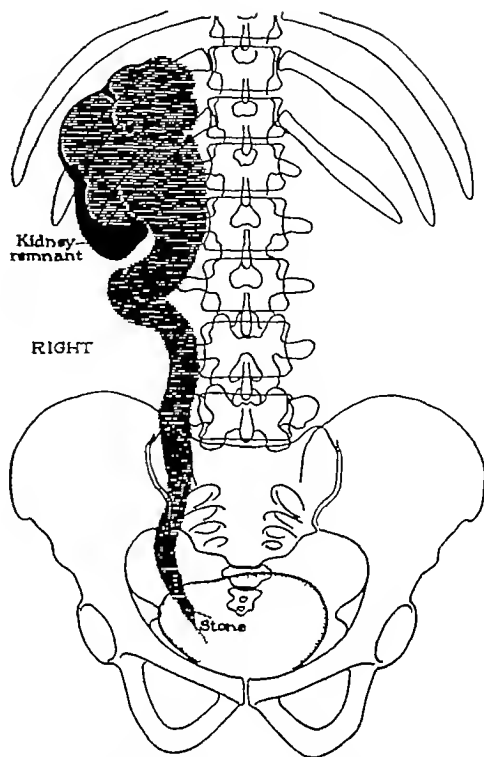


Fig. 10. Small calculus in the pelvic ureter which led to complete hydronephrotic atrophy of the kidney.

In case a patient is suffering from pain and the roentgenogram discloses a stone in the pelvic ureter, I am firmly convinced that cystoscopic examination and manipulation should not be resorted to immediately. The fact that the stone has progressed so far downward is one point in its favor for passage without instrumentation.

In this series of patients 44.3 per cent passed the stone after manipulation.

Operative treatment. As may be seen by a perusal of the literature, during the past 25 years there has been a definite trend away from open operation in favor of cystoscopic manipulation. Among some of the recent publications reporting the successful removal of stone by cystoscopic manipulation may be mentioned Alyea, 82 per cent, Fowler and Champion, 76 per cent (patients having been treated in the office), Grant, 45 per cent, Mathe, 78.3 per cent, and Thompson and Kibler, 91.3 per cent.

On the other hand, some authors report a large number of open operations Higgins, 65 per cent Rockstra 47.7 per cent

The percentages will naturally vary according to one's personal point of view and also the condition of the patient and the underlying pathology will play no small part in affecting their rise or fall

1 *Large stones* In patients with a very large stone it is perfectly obvious that manipulation is useless and that ureterolithotomy should be done at once

2 *Multiple stones* In case the patient has only 2 or 3 stones without complications one might wait or try manipulation before resorting to open operation However when complications are present operation is probably the best procedure although I have seen patients with multiple stones pass them spontaneously (Fig 9)

3 *Location* A relatively large stone high in the ureter had best be operated on whereas, if it has descended into the pelvic ureter operation may be deferred awaiting developments

4 *Duration of symptoms* If the onset of the symptoms is recent one may wait, but if there have been recurrences without signs of remission, operation is clearly indicated

5 *Reaction to instrumentation* In case severe reactions such as pain, chills, fever, hematuria, etc. occur following each instrumentation, the patient should be operated on To persist with manipulations under such circumstances is poor surgical judgment

6 *Repeated attacks of hematuria* Operation is the only procedure in case of severe attacks of hematuria, either with or without colic, accompanied by a marked secondary anemia. On the other hand, when the patient has only an occasional loss of blood and a mild secondary anemia operation may be deferred to a later date

Associated infection Severe infection in the kidney clearly indicates operation. Chronic pyelonephritis persists in these patients because of poor renal drainage and should manipulation fail operative removal of the stone is in order Acute infection, unrelieved by ureteral catheter drainage necessitates operation at once

8 *Anuria* If the stone is large, this condition should be met with immediate removal If small ureteral catheter drainage should be the procedure In case catheter drainage does not give prompt relief operation must be performed at once

9 *Suppression of function above the stone* This does not call for immediate operation, since the opposite kidney is able to carry on. I recently saw a patient who had no secretion of dye above the stone for days. She subsequently passed the stone without manipulation and the gratifying result was a complete return of function

10 *Function of the kidney* When a complete hydronephrotic atrophy exists above the stone, operation should be performed (Fig 10) When a moderately advanced hydronephrosis is present the stone should be removed to prevent further progress of the hydronephrosis but this statement should not be construed as a demand for immediate surgical removal of a stone because of the concomitant hydronephrosis which is so commonly noted in such cases

11 *Age of patient* In the older group operation is naturally deferred unless some of the previously mentioned acute, complicating conditions are present which make operation imperative

As previously stated the number of operations performed in a reported series depends upon many factors as does the type of operation that is done

In this series 114 patients, or 35 per cent, had surgical procedures as listed in Table IV

TABLE IV

Procedure	No. patients	Per cent
Ureterolithotomy	74	64.9
Pyelotomy		10.5
Suprapubic cystostomy	9	9.6
Nephrectomy	3	2.8
Nephroureterectomy		6
Embolectomy and ureterectomy		1
Resection of kidney		7
Type of operation not stated (performed elsewhere)	—	—
Total	4	90

SUMMARY

1 A series of 500 unselected patients with stone in the ureter is reported.

2 Roentgen-ray findings were positive in 95.79 per cent

3 Attention is called to the danger of certain types of manipulation

4 The advantages of the use of the ureteral catheter for dilatation and the injection of oil are considered

5 The study discloses that 128 patients passed their stones without treatment, 106, with manipulation, and 114 were operated on

6 Dangers of too frequent manipulation are stressed

7 Policy of "watchful waiting" in the average case is still desirable

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THE PHENOMENON OF ASPHYXIA RESUSCITATION

I Resuscitation with Inert (Asphyxiating) Gas in Advanced Asphyxia

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RESUSCITATION in asphyxia is of considerable and mutual interest to physiology and medicine. From the practical standpoint the problem is important in the operating room—cessation of respiration and of circulation or both—in industrial surgery—electric shock, cave-in gases and fumes—in civilian life—carbon monoxide asphyxia, drowning—and military surgery—crushing injuries, air raid casualties, war gas poisoning thoracic trauma.

Yet much controversy still exists on methods of resuscitation. For this reason we have carried out an experimental investigation in an attempt to clarify this important problem. During this work we observed a phenomenon (3) to our knowledge hitherto not described, which bears directly on the practical aspects of resuscitation. We wish now to elaborate on this phenomenon its mechanism is the subject of a paper to follow. Briefly the phenomenon of asphyxial resuscitation consists in the ability quite regularly to restore the circulation and respiration in advanced asphyxia, *without benefit of oxygen* through the use of rhythmic inflation of the lung with an inert gas alternating with rhythmic suction. That is to say in the third stage of asphyxia—cessation of respiration and rapidly falling blood pressure—resuscitation of the heart and respiration can be produced by rhythmic alternating inflation and suction with an inert gas—nitrogen helium—which has just been previously used to produce the asphyxia. Resuscitation with neutral gas is possible after obstructive asphyxia (Table I Figs 1 2 3 and 4)

Asphyxia has been divided into four stages (1) initial apnea, dyspnea, cessation of respiration or terminal apnea, and arrest of the heart. Although it is convenient to consider the total duration of acute asphyxia is approximately 4 minutes, with each stage occupying about a minute, the duration of each stage and the total time may vary. The stages can be summarized as follows

1st stage initial apnea The breath is held and the blood pressure rises.

2nd stage dyspnea Breathing is labored. The blood pressure continues to rise. At the end of this period consciousness disappears. Tonic and clonic convulsions occur.

3rd stage terminal apnea The respiration ceases. Reflexes and muscle tonus disappear. The animal is relaxed and limp. The blood pressure falls progressively toward the end of the stage the character of the pulse changes the heart beat is irregular and the blood pressure rapidly approaches zero. The sphincters are relaxed and the corneal and glottis reflexes are absent.

4th stage arrest of the heart

It should be kept in mind that due to the fact that anesthesia was given and asphyxia produced in some cases by inhalation of inert

TABLE I—SUMMARY OF 106 EXPERIMENTS WITH DIFFERENT RESUSCITATIVE PROCEDURES

	Oxygen			Chloroform		
	Sec. time	Fail. %	Per cent. success	Sec. time	Fail. %	Per cent. success
Manual artificial respiration			14			17
Rhythmic suction			10		10	
Rhythmic suction			10			
Resuscitation (rhythmic inflation and suction)		91	9	92	8	92

With the Technical Collaboration of Eugene Ostrow
From the Laboratory of Surgical Research, the Department of Surgery, and the Thoracic Surgical Service, The New York Medical College—Flower and Fifth Avenue Hospitals.

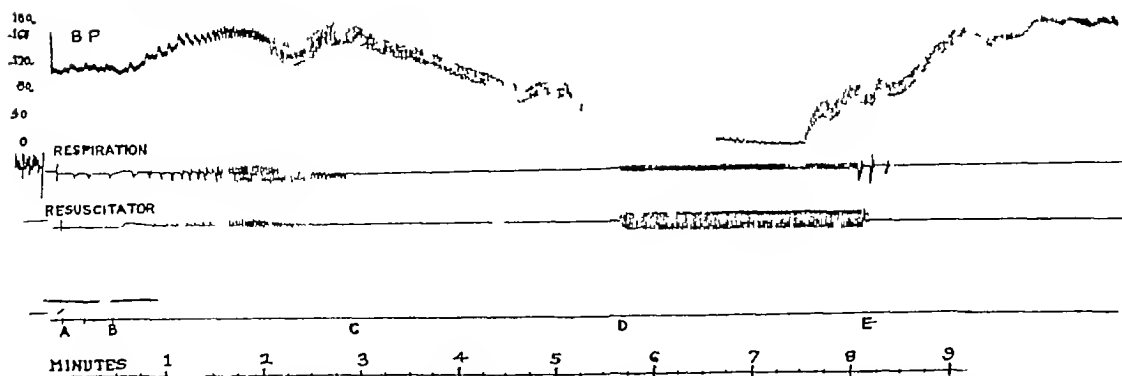


Fig 1 The phenomenon of asphyxial resuscitation *A*, Control tracing, *B*, nitrogen inhalation asphyxia, by way of leakproof intratracheal tube, begun, *C*, respiration has ceased, *D*, resuscitator—suck and blow, plus 14 millimeters

of mercury, minus 9 millimeters of mercury with nitrogen started, *E*, blood pressure is rising rapidly and spontaneous breaths occur. Resuscitator is discontinued and tracheal tube is opened to the atmosphere

gases, the stage of initial apnea may not be very evident or may even be absent

It is pertinent to consider the question of spontaneous resuscitation in asphyxia and at what point after the asphyxial procedure is stopped spontaneous recovery is still possible. Coryllos considered that if submersion is interrupted before the middle of the third stage, spontaneous resuscitation is always possible, he considered that in obstructive asphyxia "Removal of the obstructing agent before the

end of the third phase is followed as rule by immediate spontaneous resuscitation"

Since he considered his stages to occupy about a minute, this would place the critical point for spontaneous recovery under 30 seconds from the time respiration ceased in the case of submersion asphyxia and under 45 seconds from the cessation of respiration in the case of obstruction asphyxia. Loughheed, Janes and Hall, in a study on asphyxia by drowning and tracheal obstruction, have found that

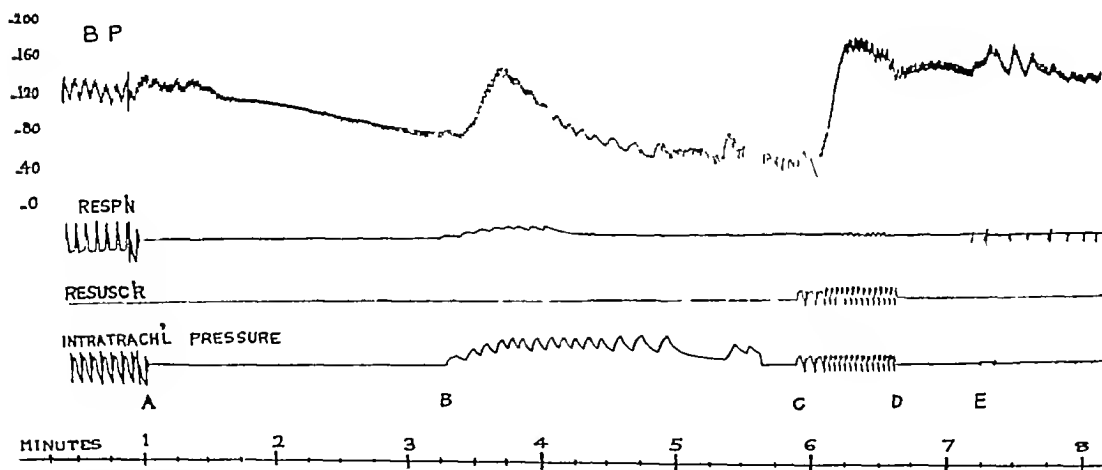


Fig 2 Asphyxial resuscitation by rhythmic pressure and suction on the lungs after failure of rhythmic inflation alone. The animal has been asphyxiated by mechanical obstruction of a specially fitted face mask, *A*, Respiration has just ceased, *B*, rhythmic inflation of the lung (14 millimeters of mercury) is begun. Since an amply large pharyngeal airway is in place, failure of the intratracheal pressure

to return to the base line may indicate a lack of tonus or adequate elastic recoil of the chest on release of the inflating pressure. *C*, Rhythmic inflation has failed to sustain the blood pressure or to initiate spontaneous respiration and the positive negative resuscitator with nitrogen is therefore applied, *D*, resuscitator discontinued, *E*, spontaneous respiration begins

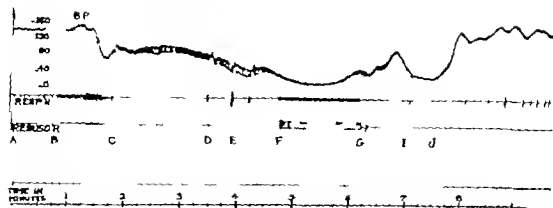


Fig. 3 A control, B helium inhalation asphyxia by occlusion of intratracheal tube, C respiration has ceased D and E, Agonal asphyxial gasps, F to G re-

ventilator with helium in action, G, tracheal tube opened to atmosphere, H, spontaneous respiration begins; I, sharp rise of the blood pressure occurs

after cessation of respiration there is a critical point at which the heart beat ceases to be expellable. In general the period between the point at which respiration ceased and the point at which the asphyxial procedure was stopped could not exceed 18 seconds if spontaneous recovery were to take place. If this period was extended even a very few seconds longer resuscitation even with manual artificial respiration together with inhalation of oxygen-carbon dioxide was impossible.

Asphyxial resuscitation with inert gas, however is effective far beyond the point at which spontaneous recovery could take place by the cessation of the asphyxial procedure. Generally we have started asphyxial resuscitation well over 45 seconds after cessation of respiration at the variable critical point at which the heart action becomes markedly altered and irregular. The length of time which may elapse after respiration ceases before asphyxial resuscitation is successfully

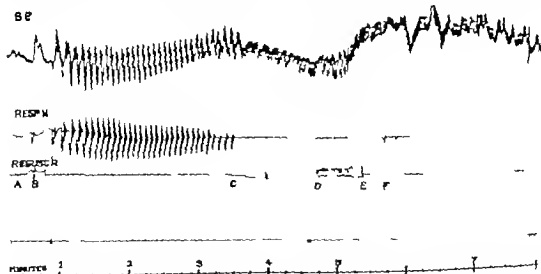


Fig. 4 A control, B mechanical obstruction asphyxia begun by clamping intratracheal tube; C, respiration ceases, D, re-ventilator with nitrogen begun, E, re-ventilator dis-

continued but between E and F the lung is connected only with an atmosphere of nitrogen, F, spontaneous respiration begins and tracheal tube opened to the air

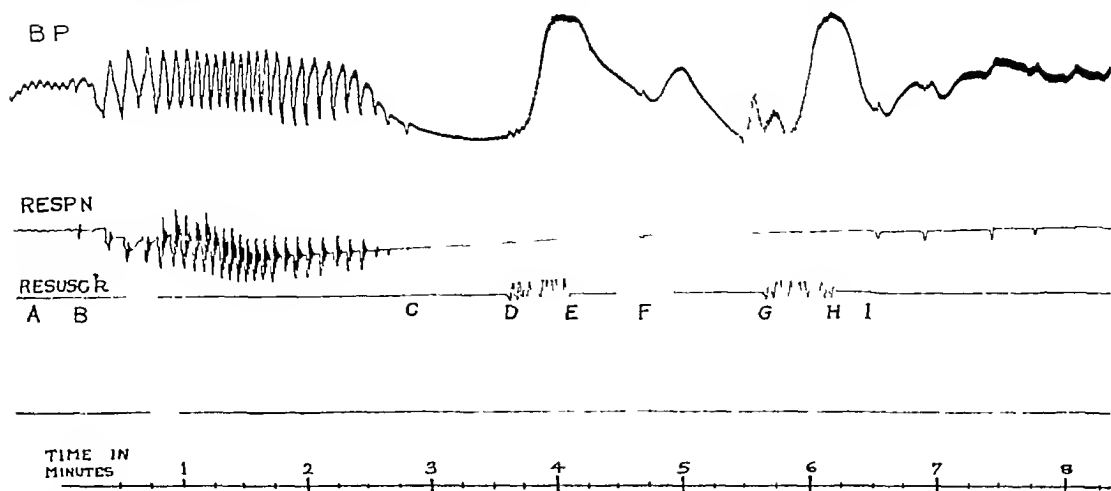


Fig 5 The vagus nerves were exposed in the mid neck and surrounded for a distance of 1 centimeter with pledgets of cotton soaked with 2 per cent procaine, for a period of 20 minutes *A*, Control curves, *B*, mechanical obstruction asphyxia begun by clamping intratracheal tube, *C*, respiration ceases, *D*, obstruction released and resuscitator with nitrogen started, *E*, resuscitator discontinued and the

tracheal tube opened to an atmosphere of nitrogen only, *F*, a spontaneous respiration is taken, *F* to *G*, lung is still connected only to nitrogen Resuscitator with nitrogen started again at *G* and continued to *H* *H* to *I*, Lung connected only to nitrogen At *I*, a spontaneous respiration is taken and tracheal tube opened to atmosphere Vagal fibers probably partially anesthetized in this experiment.

instituted varies with different experiments, the longest interval was $2\frac{3}{4}$ minutes Lastly, although in a classical asphyxial resuscitation the resuscitator¹ is kept in action not only until the circulation has recovered but also until spontaneous respiration is taken, this is not always imperative Once the resuscitator has produced recovery of the circulation as indicated by a marked or progressively rising blood pressure, spontaneous respiration can follow after the resuscitation is discontinued (Figs 2, 3, and 4)

TECHNIQUE

Dogs weighing 8 to 12 kilograms were anesthetized by the intraperitoneal injection of veterinary nembutal, 1 cubic centimeter per 5 pounds The animal was then placed on its back In some experiments, a pharyngeal airway was inserted and a specially fitted metal face mask with inflation cuff on its rim was applied In others, there was inserted an intratracheal tube surrounded by an inflatable rubber cuff to make the trachea leak-proof Asphyxia was produced either by obstructing the face mask completely or clamping the intratracheal tube In other experiments

asphyxia was produced by inhalation of inert gases such as nitrogen or helium

Tracings on the kymograph were produced by recording mercury manometers which registered the blood pressure, respiration (intrapleural pressure), intratracheal pressure and resuscitator pressures Blood pressure was recorded from the cannulized femoral artery Intrapleural pressure or respiration was recorded by means of a fine brass intrapleural cannula

For mechanical resuscitation the Emerson resuscitator was used This apparatus inflates to 14 millimeters' mercury pressure and aspirates to minus 9 millimeters' mercury pressure, it was usually regulated to make 16-20 complete excursions or respiratory strokes per minute It was connected when needed to the face mask or intratracheal tube, as the case might be Where it was desired to use rhythmic pressure alone or rhythmic suction alone on the lungs, the desired pressures were regulated by under-water glass tubing Rhythmic pressure with a gas was given at plus 12 to 14 millimeters' mercury pressure with release to 0 millimeter mercury pressure—atmospheric pressure—of the gas Rhythmic suction on the lung was carried out at

¹Emerson model

minus 8 to 12 millimeters mercury pressure with release to 0 millimeter mercury pressure—atmospheric pressure—of the gas. Manual artificial respiration was done by bilateral manual compression of the chest by the four fingers and palms of the hands at the same time that the thumbs and thenar eminences compressed the abdomen over the epigastric region. It was carried out moderately vigorously, the lungs being in communication with an atmosphere of the particular gas in question.

Inhalation asphyxia by inert gas was carried out with an arrangement to prevent re-breathing carbon dioxide since this latter gas would make the problem more complex. We called this "blow-off" inhalation asphyxia and it was accomplished by leading the expired air through the expiratory tube of the inhalator under a 5 centimeter depth of water.

ANALYSIS OF STUDY

As a precaution against the possibility of spontaneous resuscitation it was seen that asphyxial resuscitation was carried out well past the points designated as critical for such recovery by Loughbreed, Jones and Hall and Coryllos. Moreover our own control experiments have showed us that asphyxial resuscitation is possible far beyond the period at which spontaneous recovery is possible. What is more when the respiration has ceased in asphyxia, if the lungs are left in communication with 100 per cent inert gas, asphyxia will proceed to a fatal conclusion yet, the same inert gas administered by suck and blow to the lungs insures a high percentage of recovery. Such recovery is, therefore essentially inherent in the method itself for the application of other resuscitative procedures yields only a small percentage of success (Table I).

Asphyxial resuscitation with the same inert gas previously used to asphyxiate appears the more remarkable but it is also possible after mechanical obstruction asphyxia (Figs. 2, 4).

While the mechanism of the phenomenon will be discussed in a later paper it can be

surmised that the success or failure of the procedures used (Table I) bears a definite relation to the ventilatory excursion of the lung both above—inflation—and below—suction—the phase of passive expiration of the chest. In advanced asphyxia there is loss of muscle tonus and elastic spring of the chest. Manual artificial respiration is the least effective of all the procedures probably because it, more than the other procedures used, depends chiefly on the elastic spring of the chest for pulmonary ventilation. On the other hand positive—negative resuscitation, which gives the most effective ventilatory excursion independently of the state of tonus of the chest, also gives by far the greatest percentage of successful resuscitation with inert gas.

Perhaps most surprising of all is the fact that suck and blow resuscitation with inert—asphyxiating—gas is more effective than manual artificial respiration with oxygen inhalation. We do not mean to infer by these observations that inert gas should be used clinically. For clinical purposes the use of oxygen or oxygen-carbon dioxide is indicated as preferable.

SUMMARY

Advanced asphyxia was produced experimentally by tracheal obstruction or inhalation of inert gases—nitrogen helium. When, in such asphyxia the respiration has ceased it is possible to resuscitate with a suck and blow apparatus, inert gas being used. Such resuscitation is possible in a high percentage of cases and far beyond the period at which spontaneous recovery could occur by discontinuing the asphyxial procedure. With other methods of resuscitation—manual artificial respiration rhythmic inflation rhythmic suction—recovery of the circulation and respiration is the exception rather than the rule.

In this phenomenon of asphyxial resuscitation the heart and circulation recover first, the respiration later. Typically applied in experimental asphyxia the positive-negative resuscitator with inert gas, is kept in action until the blood pressure has definitely recovered and spontaneous respiration is taken when the lungs are left in communication with

¹On the paper to follow blood oxygen levels simply verify the outcome experimental asphyxia produced.

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THE SIGNIFICANCE OF THE GALACTOSE TOLERANCE TEST IN HYPERTHYROIDISM

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THE galactose tolerance test has been used by a few investigators to confirm the diagnosis of hyperthyroidism. Our interest was directed toward the correlation of this test with the clinical and pathological diagnosis of hyperthyroidism and the basic metabolic rate.

Althausen and his co-workers (1, 3) and MacLagan and Rundle (8) found the results of this test very much in accord with both the clinical and pathological diagnosis. Althausen, on the basis of animal experiments and clinical investigation with galactose tolerance tests, states that the principal factor in high galactose readings in hyperthyroidism is due to increased intestinal absorption resulting from stimulation of the intestinal mucosa by thyroxin. The investigations of MacLagan (7) and Lichtman lead them to believe that hepatic dysfunction is the basis for abnormal tolerance. From our observations certainly the latter is true, for positive findings occurred in patients with known liver damage and without hyperthyroidism. The hypothesis of Althausen is also true to some extent as verified by a few of our findings, namely that in 4 cases of myxedema the galactose tolerance was below normal in all, and in 6 out of 18 cases with hyperthyroidism there was some galactose in the blood between the 5 and 15

minute intervals after the administration of galactose.

That increased intestinal absorption is not the underlying factor is stated by Lichtman inasmuch as 54 per cent of his patients with thyrotoxicosis gave normal galactose curves. His test consists in the oral administration of galactose and the analysis of the urine for the presence of this sugar. In response to this technique MacLagan and Rundle agree that in patients with known liver damage this analysis gives many negative results. Lichtman's theory for the liver being the sole factor in elevated galactose readings is that the glycogen and the carbohydrate reserves, and to some extent the protein reserve of the liver, are exhausted. The hepatic cells are then left without protection and are vulnerable to various toxins, intermediate products of metabolism, and thyroxin.

In a discussion of the various tests of hepatic function, Snell and Plunkett believe that the galactose tolerance test, because of its simplicity and the relatively satisfactory results, is an exceptionally good test in determining liver functions. There are, however, good reports in the literature concerning the use of the hippuric acid test in hyperthyroidism (4, 5, 10). Mann is of the opinion that inasmuch as the utilization of galactose appears to depend mainly on the liver, it should be possible to indicate hepatic injury by the tolerance test. But others (11) have stated that the galactose tolerance test is of

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little value in determining hepatic damage. We agree with Haines and associates that the test is not of great value in the management of hyperthyroidism, since it interprets liver damage in terms of liver function.

The galactose tolerance test is based on the fact that galactose is removed from the blood stream chiefly by the liver and is presumably converted into glycogen (Mann). Galactose is used in preference to glucose because it is much more readily and easily determined in the blood.

The technique of this test, as used by us, consists in the oral administration of 40 grams of galactose dissolved in water to a patient who has fasted for 12 hours. Specimens of venous blood are obtained before the administration of the sugar and 30 and 60 minutes afterward. In most of our cases the 120 minute specimens were also taken but infrequently the 5 and 15 minute specimens. The glucose fraction is removed by fermentation after the method of Folin Wu and the remaining filtrate is titrated as glucose. This quantity in the fasting specimen is then subtracted from the corresponding figure in subsequent specimens. Inasmuch as the galactose has a lower reducing power than glucose 24 per cent may be added to the readings of the nonfasting specimens.

Our series was composed of 98 consecutive cases manifesting some or many of the symptoms of thyrotoxicosis. These patients had been admitted to the Hutchinson Memorial Clinic of Tulane University Medical School, the Tulane Surgical Divisions of Charity Hospital, and Touro Infirmary. After completion of the clinical and laboratory studies, 75 of these patients were advised to undergo a thyroidectomy. Eleven of these patients have not been operated upon as yet and as long as the diagnosis has not been established by pathological examination these cases are not included except to mention that all had elevated galactose readings and all but 3 had elevated basal readings.

The average normal as taken from 10 medical students tested was 16 or milligrams per cent at 30 minutes, 7.10 milligrams per cent at 60 minutes and 1.61 milligrams per cent at 90 minutes. The highest reading was

41 milligrams per cent and the lowest was 9 milligrams per cent.

The following 87 cases are listed as to their final diagnosis. Those with positive galactose tolerance test: hyperthyroidism 41 cases nontoxic goiter after iodine 3 cases hypertensive cardiovascular disease 2 cases menopausal syndrome 1 case syphilitic cirrhosis of the liver 1 case urticaria, 1 case amebiasis, 1 case catarrhal jaundice 1 case dyncbondroplasia, 1 case.

Galactose below the normal level occurred in myxedema 4 cases nontoxic nodular goiter 4 cases arteriosclerotic heart disease 1 case peptic ulcer 1 case neurocirculatory asthenia, 1 case.

Normal galactose curves were found in nontoxic nodular goiter 8 cases nontoxic diffuse goiter 3 cases thyroid adenocarcinoma, 2 cases familial jaundice, 1 case hypertensive cardiovascular disease 2 cases amebiasis, 1 case anxiety hysteria, 1 case manic depressive psychosis, 1 case cystic goiter 1 case colloid goiter 1 case toxic nodular goiter 1 case.

Of the 64 patients operated upon the histopathological report was diffuse toxic goiter 28 cases nodular toxic goiter 14 cases nontoxic nodular thyroid 12 cases nontoxic diffuse thyroid 3 cases adenocarcinoma (thyroid) 2 cases nontoxic (after iodine) 3 cases cystic goiter 1 case colloid goiter 1 case.

Relationship of the preoperative tests: 1 cases of toxic goiter are listed in Table I.

TABLE I

Pathological diagnosis	Cases	Basal metabolic rate	Galactose Tolerance test
Toxic diffuse goiter	43	+32	30 17
Toxic nodular goiter		Mean +45	Mean 43 5 50
Nontoxic (after iodine)		+4	4 8 6

case with normal basal metabolic rate and galactose tolerance.

The 3 cases reported as nontoxic after iodine are recorded here under the toxic cases because the pathologist's report stated that the gland showed a histopathological picture characteristic of remission. The admi were

dilated with colloid but there was no marked hyperplasia present

Of the 42 cases of toxic goiter there were 10 cases in which the basal rate was within or below the accepted limits or normal. The lowest basal metabolic rate of this group was -4 , and the highest $+71$. All of the cases of toxic goiter except one had a positive galactose tolerance curve. This was a case of toxic nodular goiter with a basal metabolic rate of $+5$, and galactose readings of 20 milligrams per cent and 39 milligrams per cent at the 30 and 60 minute intervals, respectively. This patient had been taking iodine and sedatives for 3 months prior to admission to the clinic. Operation was advised in this instance on the basis of the clinical manifestations.

Pathological diagnosis of nontoxic goiter as related to preoperative tests are given in Table II.

TABLE II

Pathological diagnosis	Basal metabolic rate	Galactose tolerance test	
		30 min	60 min
Cystic goiter	-2	37	30
Colloid goiter	$+30$	75	41
Nontoxic diffuse goiter	$+3$	32	26
	$+12$	14	22
	-3	12	12
Nontoxic nodular goiter	$+8$	16.5	13.5
(Mean of 12 cases)	$+27$	23.5	2.3
Adenocarcinoma	$+24$	5	12

In the 1 case of cystic goiter the patient presented all of the symptoms of hyperthyroidism. The basal metabolic rate was low but the galactose readings were on the upper border of normal. The case reported as colloid goiter gave high readings for both the basal metabolic rate and the galactose tolerance. In each of these cases a preoperative diagnosis of diffuse toxic goiter had been made, and it is our opinion that premedication had changed the pathological picture.

There are 2 cases in which the efficacy of the galactose tolerance test is particularly revealed. The first case is that of a 33 year old white female who entered Touro Infirmary with the complaint of frequent headaches and the progressive loss of weight for about a year. Physical findings revealed only evidence of weight loss and tremor of the fingers. There was no exophthalmos or apparent enlarge-

ment of the thyroid. The pulse rate was 100 and the basal metabolic rate -4 . The galactose tolerance test readings were 116 milligrams per cent at 30 minutes and 85 milligrams per cent at 60 minutes. After diligent study the patient was subjected to a thyroidectomy. The pathologist's report after examination of the gland was toxic nodular goiter. Since the operation the patient has been free of symptoms and has gained weight. This case showed the most marked discrepancy between the basal metabolic rate and the galactose tolerance test.

It is here that the test has its greatest significance, i.e., the test will aid in confirming the diagnosis in patients with symptoms suggestive of thyrotoxicosis and who have a normal basal metabolic rate.

The other example which illustrates the value of this test is that of a 42 year old female who 2 years previously had had a thyroidectomy. The clinical and pathological diagnosis was toxic goiter. However, the patient had no relief of symptoms following the operation. She was again admitted to the hospital. The basal metabolic rate was slightly elevated and the galactose tolerance test was high. It was suggested that the patient might have a mediastinal goiter. Roentgen examination of the chest and subsequent operation confirmed this diagnosis. Following the last operation the patient had no more toxic symptoms.

The galactose tolerance test should not be used to replace the basal metabolic determinations in patients with suspected hyperthyroidism for in most instances the basal metabolic rate and the galactose test will be elevated above the normal and the basal metabolic rate will be more likely to indicate the severity of the toxicity, especially when the readings are high. Two examples of this occurred in our series. One fatality due to postoperative thyroid crisis had a preoperative basal metabolic rate of $+64$ and tolerance readings of 57 milligrams per cent and 79 milligrams per cent. Whereas a comparatively uneventful convalescence following hemithyroidectomy (first stage) was manifested by another patient whose preoperative tests revealed a $+27$ basal metabolic rate and galactose readings of

167 milligrams per cent and 200 milligrams per cent. The last mentioned galactose test had the highest reading of the series. The lowest was 44 milligrams per cent at 30 minutes and 6 milligrams per cent at 60 minutes.

In the toxic group of cases there was no correlation between the basal metabolic rate and the galactose tolerance test. There was also no correlation between the duration of the disease and the galactose tolerance test, for in some instances the galactose readings were high when the hyperthyroidism had been clinically of short duration and in other instances the test was low when the disease had been present for a long period of time. When the patient with hyperthyroidism shows a good clinical response to preoperative management and premedication the galactose curve tends to approach the normal but not in direct proportion to the basal metabolic rate. Following thyroidectomy the galactose curve gradually returns to normal, which suggests that in thyrotoxicosis liver dysfunction is not as a rule permanent.

In summarizing this investigation, it may be stated that the galactose tolerance test used in conjunction with the basal metabolic rate can be of definite aid in confirming the diagnosis of hyperthyroidism. Too much confidence can not be placed in any one test, nor can a test replace clinical experience or diagnostic ability. The responsibility for decision as to the course of therapy depends not on the results of the tests *per se* but does depend on the judgment of the physician.

In 41 of 46 cases, in which the preoperative diagnosis was toxic goiter the diagnosis was confirmed by the galactose tolerance test. All of the 5 exceptions had a preoperative diagnosis of toxic goiter. It is our opinion that in these 5 cases, because of premedication or prolongation of the disease the pathological picture had changed from typical toxic characteristics to a modification of this state. The cases of nontoxic nodular goiter after iodine cystic goiter and colloid goiter in all of which the preoperative diagnosis was toxic goiter probably showed the pathological condition as the result of premedication or in the case of cystic goiter prolongation of the disease.

In conclusion it is well to stress the fact that wherein the basic metabolic readings are within normal limits in patients manifesting symptoms of thyrotoxicosis, the galactose tolerance test will be of great aid in confirming a diagnosis of hyperthyroidism.

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CHRONIC IDIOPATHIC ULCERATIVE COLITIS

Report of Seven Cases of Patients Operated Upon

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THERE is an ill defined but important group of patients who present ulceration of the large bowel with no recognizable causal agent. For this condition there is at present no specific therapy.

The disease varies in violence within wide limits. Its onset may be sudden, and its severity so great as to cause death within a short time. Or its severity may be less, with few symptoms present, despite decided pathological changes. The most common and striking clinical characteristic is the tendency to chronicity with recurrent mild to severe exacerbations. McKittrick and Miller, in their analysis of 149 cases, describe one case with five separate recurrences in 1 year, and another patient who had 12 years of freedom between attacks. It is small wonder then that a wide difference of opinion exists as to the relative merits of various modes of therapy and as to the results obtained in any particular type of treatment.

The disease tends to involve all of the bowel wall, so that the muscularis becomes markedly thickened and the serosa is edematous and injected. The mucosal surface is denuded to greater or less degree and healing results in scar, with or without "heaping up" of islands of mucosa (to which the term pseudopolyposis has been applied), and in strictures. Healing of the muscular coat also results in fibrosis with loss of muscular tone and narrowing of the lumen of the bowel.

The disabilities of the disease are serious. Some patients suffer recurring attacks of fever and prostration, others are handicapped by continuous symptoms, of greater or less severity, and loss of weight and strength over prolonged periods. The loss of normally functioning mucosa causes faulty absorption, and, together with loss of food by diarrhea, results in nutritional deficiency. The infected colon acts as a focus of infection, frequently causing

multiple arthritis, and eye complications such as keratitis, iritis, and corneal ulcers. We have seen a young woman who lost the sight of one eye as a result of the disease.

Complications are common.

1 *Perforation* usually leads to death from generalized peritonitis. Abscess and fistula formation are fairly frequent. Barger (5) reports the incidence of perforation as 3.4 per cent in a total of 647 cases. In 10 of 18 cases, the perforation was located in the sigmoid. Perforation also occurred in the cecum, rectum, and splenic flexure. Multiple perforations were found in 2 cases. He reports a case of colojejuno gastric fistula in a case of infantilism. He attributes the infantilism to the onset of the disease at an early age with lack of absorption of vitamins and mineral substances. Studies ruled out other known forms of infantilism.

2 *Massive hemorrhage* has been encountered by all writers. McKittrick and Miller report an incidence of 5 per cent in their cases.

3 *Strictures and narrowing of the lumen* occur in cases of long standing. Cattell (10) reports 2 cases in which complete obliteration of the lumen occurred at one or more points. In 4 of his patients stricture formation in the rectum was so extensive that a digital examination beyond the anal sphincter was impossible. We observed the same condition in one of our cases.

4 *Pseudopolyposis*. There is some difference of opinion as to the relationship of pseudopolyposis to chronic ulcerative colitis. Barger and Comfort (4) report an incidence of 10 per cent pseudopolyposis in 693 cases of chronic ulcerative colitis. They state that of every 5 cases of multiple polyps of the colon studied at the Mayo Clinic, 4 are on the basis of chronic ulcerative colitis. Barger (2), in another communication, reported an incidence of 13 per cent in 200 cases. Bancroft believes

that polyposis may be a part of the healing process, but David contends that it is definitely not part of the healing process. Bagen (2) states that the development of polyps is noted proctoscopically in the course of progressing as well as healing chronic ulcerative colitis. The possibility of malignant degeneration in these polyps is a matter for serious concern. Rankin (21) reports 25 cases of carcinoma in 1100 cases of colitis, an incidence of 2.3 per cent. Brust and Bagen report an incidence of 2.5 per cent in 800 cases. In contrast they quote the statistics of the United States Department of Commerce which indicate that 0.011 per cent of persons die from carcinoma of the intestine, and those of the Mayo Clinic which indicate an incidence of 0.88 per cent of carcinoma of the large intestine in all patients registering at the Mayo Clinic.

5. *Thrombophlebitis and mesenteric thrombosis and 6. colonic intussusception.* Among the rarer complications which have been reported are thrombophlebitis and mesenteric thrombosis (Cave 12) and colonic intussusception (Bagen 5).

It is important that we consider two other features of the disease: namely its diffuse nature and its tendency to spontaneous remissions and exacerbations. Bagen and Mayo (6) report that in 95 per cent of 1500 cases of chronic ulcerative colitis the disease process began in the lower portion of the rectum and spread upward to involve the remainder of the large bowel. McKittrick and Miller report an involvement of the terminal ileum in 1.3 per cent of their cases and state that segmental colitis was rarely found. Cave and Nickel (13) found the terminal ileum apparently involved in 25 per cent of their cases yet on subsequent examination after ileostomy only 4 cases remained involved. Cattell (10) performed a loop colostomy well above the involved portion of bowel in 2 cases in which the disease was limited to the sigmoid and rectum. The disease spread through the colostomy to the proximal bowel. In one of the cases, extension occurred within 2 months. It is known that lesions may seemingly clear up entirely either spontaneously or following ileostomy, yet may become reactivated spon-

taneously or with re-establishment of the intestinal continuity. Stone (25), Lahey, Rankin (21) and Cave and Nickel (13) report reactivation of the disease in cases in which re-establishment of the intestinal continuity was made following apparent cure resulting from ileostomy. In view of these reports it is difficult to reconcile the seemingly excellent results reported by Rienhoff, Strauss and Stone (25, 26) unless it be that their cases had not been followed for a sufficient period before the reports were published.

Since no specific etiological factor has ever been proved a great many differing forms of conservative medical therapy have been attempted. Because the disease varies so greatly in its pathological findings and the severity of its symptoms widely differing results from the use of any given method of treatment have been reported. Several optimistic reports have been published which command consideration. Thus Crohn and Rosenak report a series of 90 cases, 75 of which were followed for an ample period. They claim that 75 per cent of their cases were cured or improved by medical means alone. Most of these patients were in their first 2 years of illness. Eleven per cent of their cases were unimproved, and 15 per cent died as a result of the disease. Bagen, Brown and Rankin (3) also report a similar degree of success with medical management.

The acceptance of these statistics brings us to the conclusion that medical therapy is in sufficient in about 25 per cent of these cases. We concur with Lahey, Cave, and others, that the management of this disease demands close co-operation between the internist and the surgeon. Surely no one would suggest that surgical treatment be tried before the patient has been amply treated medically, the response to such treatment evaluated, and the extent of permanent damage to the colon determined. One must also bear in mind that some patients with marked pathological changes appear to have few symptoms. We, in common with the medical enthusiasts, hope the future may bring us knowledge of the etiology of the disease and a more specific therapy. But, for the present, it is our feeling that the pathology of the disease is in many

instances irreparable Mackie in an analysis of medical management, states that when extensive anatomical changes have occurred it is vain to hope for restoration to normal Brown (8) urges surgical treatment before the ulcerations have become so deep that complete restoration of the gut to normal function is less probable Cave (12) believes it unreasonable to assume that a disease which has caused such extensive infiltration in the deeper layers of the colonic wall could be reached by any known medical procedure

We believe that surgery finds a definite place in two groups of cases, namely, the acute fulminating type, and the chronic intractable type, complicated by sequelae which in themselves are serious conditions

Strauss, Stone (25), McKittrick and Miller, and Cave and Nickel (13), have advocated the use of ileostomy in the acute fulminating cases before the patient's condition has been too greatly impaired Single-barreled ileostomy, first advocated by Brown (7), completely diverts the fecal current from the diseased bowel, and thus gives complete physiological rest to the large bowel Striking clinical improvement is seen following ileostomy, yet in most instances the toxemia, although temporarily diminished, persists We cannot expect this procedure to be curative, notwithstanding contrary isolated reports in the literature (Stone, 24, 25, Strauss, Rienhoff) Ileostomy has gained a reputation for a high mortality rate McKittrick and Miller report a rate of 28 per cent in 54 cases Kunath reports 83 per cent in 12 cases and advocates appendicostomy or cecostomy as the procedures of choice, these have resulted in a mortality of 21 per cent in 19 cases Cattell (11) reports a mortality of 22 per cent, and Cave and Nickel (13) report a mortality of 45 per cent in 11 emergency ileostomies and of 11 per cent in 19 elective ileostomies Borgen, Brown and Rankin (3) report a 66 per cent mortality in 9 emergency ileostomies and of 50 per cent in 82 elective ileostomies, 30 per cent of which were immediate, and 20 per cent late It is possible that the rapid and excessive loss of fluids immediately following surgery is a factor in producing mortality, but the more likely reason for mortality in many

instances is that surgical aid is invoked too late Cave and Nickel (13) no longer advocate ileostomy in the presence of massive hemorrhage They believe that vitamins K and C are competent to control the bleeding and that surgery in these cases almost always results fatally

We urge surgery in the chronic intractable type, in cases constantly handicapped by chronic symptoms, in cases presenting progressive extension of the pathological changes, in cases showing periods of activity and remission with extension of pathology, and in those complicated by the sequelae previously discussed

There are a number of surgical procedures which we need to discuss briefly

Appendicostomy and cecostomy have been advocated chiefly for the doubtful value of irrigation These procedures fail to divert the fecal current completely and are inadequate

Colostomy, with distal partial colectomy, is applicable only to cases of segmental colitis, which have been estimated to constitute only 10 per cent of the whole A colostomy is more desirable than an ileostomy but is very rarely indicated

Ileosigmoidostomy, with or without proximal subtotal colectomy, has been enthusiastically advocated, but we must bear in mind that 95 per cent of cases begin with rectal involvement, and that apparently healed lesions may become reactivated with re-establishment of continuity Our experience with a recent case which will be described, and with another patient treated elsewhere, who retains active lesions in the remaining bowel with multiple fistulas and widespread arthritis, and who has lost the sight of one eye, convinces us that this procedure is very limited in its applicability

Total colectomy we believe to be logical because it completely disposes of the diseased bowel, results in no permanent damage to the patient, and is attended with a reasonable mortality

Cattell (11) has reported 24 total colectomies with 3 deaths, Rankin (21, 22), 7 total with no deaths, 4 subtotal with 1 death, Cave (12) 3 total and 3 subtotal with no deaths, McKittrick and Miller 2 total and 8 subtotal

with 1 death. The aggregate totals 51 cases with 5 deaths or a rate of approximately 10 per cent. We realize that the combined group represents a small series from which to draw extensive conclusions but, granted proper management it seems that mortality should be within reasonable limits for this type of surgery.

The operation should be done in multiple stages. We will not attempt to describe in detail all of the steps. The first stage of the operation entails ileostomy the second, subtotal colectomy from the terminal ileum around to the lower sigmoid the omentum being preserved. On occasion it may be necessary to conduct two stages for this portion of the procedure, as we found in one of our cases. The third stage consists of combined abdominoperineal or posterior resection of the remaining sigmoid and rectum.

Different forms of ileostomy technique have been described by Brown (7) Rankin (21) MacGaire Cattell (11) Cave and Nickel (13) and Stone (26). These vary from an ileostomy combined with appendicostomy to implantation of the terminal stoma in the abdominal wall as a mucous fistula. We prefer the single barreled or end ileostomy turning the distal limb in and dropping it. We are not unmindful of the warning voiced by some, that stricture in the distal bowel might result in opening of the closed ileum. We have so far left the clamp on the proximal limb for 36 to 48 hours. Recently immediate tube drainage has been advised by many. We have decided to adopt this procedure in the future. We do no exploration of the abdomen at the time of performing ileostomy since little information can be gained and trauma might complete an impending perforation. The complications of ileostomy have been completely described by Cave and Nickel (13) bleeding from mucous membrane prolapse retraction narrowing of stoma, secondary openings proximal to the stoma, intestinal obstruction, pronounced colapse due to loss of sodium chloride from suden and rapid ejection of fluid from the stoma. We try to guard against prolapse by suturing the mesentery to the anterior peritoneum, but encountered this complication in one case.

Ileostomy may on occasion be an emergency procedure. The succeeding stages need never

be done in haste. Sufficient time must elapse following ileostomy to permit water balance to be re-established and general improvement of the patient's condition. A minimum of 5 to 8 weeks has been advised. Whittaker's observations on ileostomy indicate that water and mineral balance begin to be established at the end of 1 month, and that average weight and strength are regained in about 3 months. We waited 2½ years on our first patient because repeated acute exacerbations with massive hemorrhages, precluded earlier intervention.

We performed the second stage in two procedures on our second patient because she had previously suffered a perforation at the splenic flexure with abscess formation. In the first of these we resected to the splenic flexure. In the second we resected to the lower sigmoid.

We believe that at least 1 month should be allowed between the second and third stages for proper preparation of the patient. Cave (12) advocates a period of 2 to 6 months.

Our surgical experience is based on 7 patients operated upon 2 ileostomies without further surgery 4 total colectomies, and 1 ileosigmoidostomy with resection of the proximal colon.

The complications encountered were as follows (1) prolapse of ileostomy in 1 of the 5 ileostomies, which necessitated surgical correction (2) partial dehiscence of the wound following the second stage operation in 1 of the 4 total colectomies (3) dehiscence of the wound with fecal fistula following resection of the proximal colon in the patient on whom an ileosigmoidostomy was done (4) completely dysfunctioning neurogenic bladder following the third stage in the first total colectomy performed.

Since then, Dr. A. A. Kutzmann, of our urologic department, has instituted total drainage on all of our cases immediately after operation and has been successful in obviating serious bladder disturbance.

Management of the ileostomies has presented some difficulties. It has been stated that when colectomy has been completed, the terminal ileum has taken on the function of the large bowel with absorption of fluid and solidification of the stool resulting in infrequent movements. Dr. William Bachrach,



Fig 1 Diagram of cecum and ascending colon Wall markedly thickened and lumen narrowed Previous destruction of mucosa Some active ulceration Case 3, S.L

of our resident staff, made some interesting observations independent of the work of Whittaker previously mentioned. He found the intestinal passage time to be about 4 hours. Protein in the form of meat and starch in the form of potato were readily digested. Leafy vegetables, and those with distinct membranes such as peas and corn, left considerable residue. Seeds were, of course, not digested. There was no significant effect from varying the water intake. Milk resulted in a more acid, more liquid stool. Dr. Bachrach suggests the following dietary regulations: (1) No restriction of amount, but food to be taken at conventional meal times, (2) meat and potatoes as desired, (3) moderate amounts of nonleafy, nonmembranous vegetables, (4) daily intake of strained orange juice, (5) vitamin supplements may be added. By applying these rules our patients have been able to restrict the movements to three or four in 24 hours. One of the patients has been able to dispense with the wearing of a bag on most occasions.

Whittaker, in his observations on the human being following colectomy or colonic exclusion with ileostomy, has demonstrated that there are few temporary and no permanent effects on mineral metabolism, no change in the motor activity of the small intestine, some physiological dilatation of the terminal ileum, and that in 3 months patients may regain average weight and strength.

Our results in the 4 totally colectomized patients have been very gratifying to the

patients who express enthusiasm over the results and are not at all unhappy with their ileostomies.

REPORT OF CASES

CASE 1 E.R., female. Illness began in 1925 at the age of 20, with bloody diarrhea which lasted 5 weeks. In 1930 she had an attack which lasted 2 months. In January, 1934, she had an attack of influenza, and 1 month later developed bloody diarrhea which continued until her admission to the hospital on May 18, 1934. For 1 month previous to the hospital ad-



Fig 2 Showing complete replacement of mucosa by chronic inflammatory changes. Note increased submucosal fat. Case 3 S.L. X 95



Fig. 5. Barium colon enema roentgenogram reveals narrowing below the splenic flexure with distention of proximal bowel. Loss of normal pattern and haustration in the descending colon. Case 4. L.P.

mission she had 5 bloody rectal movements daily a great deal of abdominal pain, and some vomiting. She had lost great deal of weight and felt very weak. She was given whole blood transfusion on May 20, 4 days after hospital admission she appeared to have had perforation of the bowel. Exploratory laparotomy as done through a McBurney incision under local anesthesia. There was a great deal of clear serous peritoneal fluid which on culture grew *Streptococcus viridans*. A cecostomy was done. A blood transfusion was given and repeated on June 1. On June 9, there was hemorrhage from the cecostomy and rectum. The blood count dropped moderately and in 4 days Sigmoidoscopic examination revealed good many active ulcerations extending to 9 1/2 inches, there being a few ulcers in the rectum. 1 August she was transferred to convalescent home. The improvement continued to be very slow. She was readmitted to the hospital and an end ileostomy was done on September 7, 1934. Retraction of the ileostomy gradually took place and a new ileostomy was done on November 25, 1934. She improved steadily following this, gaining great deal of weight and having few rectal passages

of mucus and pus. 1 May 1938 sigmoidoscopic examination revealed acutely injected rectal mucosa which bled readily on touch. 1 May, 1939, prolapse of the ileostomy necessitated resection of the prolapsed ileum. She was last seen 1 January 1940. Her general appearance was very good. There was marked contrast between her emaciation in 1934 at the time of her first illness, and the obesity in 1940. She continued to pass mucus and pus rectally however and sigmoidoscopic examination revealed continued ulceration. She has refused total colectomy and we have refused to re-establish bowel continuity.

Almost continuous fluid drainage from the ileostomy has rendered her useless for employment and a burden on society. Despite the very evident improvement in the patient's condition activity of the disease continues.

CASE 3. M.G. male. Illness began in 1931 at the age of 35 years, with fever, painful swelling of the knees and ankles, lower abdominal cramps and bloody diarrhea. The attack lasted only a few days. He was placed on an ample medical regimen and suffered only a few mild exacerbations. In August, 1935, when he had a severe exacerbation characterized by abdominal pain, nausea, vomiting, 4 to 6 bowel movements daily, swollen tender knee joints, and great weakness. He lost 10 pounds in eight or a few weeks, and weighed 135 pounds when admitted to the hospital. His previous normal weight had been 165 pounds. Ileostomy was performed on August 4, 1935. He enjoyed remission of his illness for 1 year, weighing 180 pounds at the end of that period. For the following 5 months he again suffered from chills, fever, anorexia, vomiting, and bloody rectal movements. Multiple arthritis again became evident. Under more active medical care he improved and enjoyed another remission of 6 months duration. At the end of that time he had a mild exacerbation during which an ischio-rectal abscess developed. Since that time he has remained well except for short periods of mild exacerbation. When last seen by us January 1940, he weighed 190 pounds and felt very well. An attempt to do sigmoidoscopic examination revealed that a small finger could not be inserted into the anus. Total colectomy has been advised but refused by the patient.

Ileostomy has resulted in virtual cure of the disease from the patient's point of view. We feel, however, that in view of the anal stricture, long eventual re-establishment of bowel continuity is impossible.

CASE 3. S.L. female. Illness began in 1921 at the age of 20 years, characterized by cramps, bloody diarrhea, and vomiting. There are rare periods of remission except for persistent complete relief during pregnancies in 1933 and 1935. About 1933, she developed multiple arthritis, involving practically all joints, at times necessitating the use of crutches.

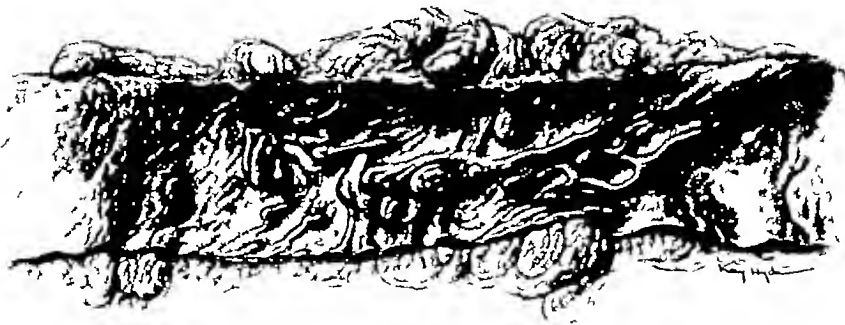


Fig 4 Diagram of section of colon reveals complete loss of normal mucosa with scarring. Some surviving islands of mucosa appear to be proliferative, producing pseudopolyposis. Case 4, E P

had an exploratory laparotomy and appendectomy in 1933. In 1934, a cecostomy was done elsewhere. She improved for 1 year and again developed cramps, bloody diarrhea, and arthritis of moderate severity, with periods of remission. She had been cared for by a great many physicians in this community. We saw her in 1936 and performed an ileostomy in March of that year. Her symptoms and general condition improved. She gained some weight, but her arthritis continued to be bothersome, and she began to have more purulent and bloody drainage from the bowel, in addition to a good deal of abdominal pain. In the spring of 1937 she was sent into the hospital and was being prepared for colectomy, when she developed a most acute exacerbation, having massive hemorrhages from the bowel and much pus. She was treated conservatively. She weighed 80 pounds when she left the hospital. Her normal weight had been about 130 pounds. During the illness she had weighed on the average 95 to 100 pounds. She improved and gained weight but continued to pass pus and blood by rectum.

On July 26, 1938, first stage colectomy was done, the bowel being resected to the sigmoid. One month later, on August 25, 1938, the abdominoperineal resection was done. This patient developed the bladder difficulty previously mentioned. It has been considerably improved under treatment. It is now 28 months since the completion of colectomy. The patient feels extremely well. She has had to restrict her diet because she now weighs 146 pounds, which is approximately 16 pounds over her previous normal weight. The ileostomy is satisfactorily controlled.

The specimen revealed marked thickening of the wall with narrowing of the lumen (Fig 1). The mucous membrane appeared to be almost completely absent and there was some active ulceration in the remaining mucosa. The microscopic sections revealed severe chronic inflammatory change, with ulceration of the mucosa and hypertrophy and fibrosis of the muscularis (Fig 2).

This patient had had repeated exacerbations and remissions for 14 years before ileostomy. The most severe exacerbation occurred 1 year after ileostomy was performed, and at the completion of total colectomy, 2 years after ileostomy, active ulceration was found in the specimens. She remarried 2 months ago.

CASE 4 E P, female. Illness began in 1929 at the age of 21 years, characterized by severe bloody diarrhea. She had rather frequent attacks of moderate severity. In 1931 she was delivered by cesarean section and shortly developed a right tubo ovarian abscess which necessitated surgery. Although the colitis was particularly bothersome during the pregnancy, there appeared to be a remission until the next pregnancy in 1933, when she was again delivered by section. The colitis was moderately active during this pregnancy. In 1936 she suffered a severe attack which necessitated hospitalization. This was the fourth severe attack. The illness continued mild until July, 1938, when she developed pain in the left loin and flank accompanied by high fever. This subsided after several weeks. Subsequent x-ray study revealed narrowing below the splenic flexure with penetration at this point (Fig 3). The evidence of obstruction with cramps accompanied by visible peristalsis became more marked and for a matter of 2 weeks the patient was in great distress. In September she developed a diarrhea, having about 6 or 8 watery stools daily, and she became nauseated. She was admitted to the Hospital in October but continued to lose ground, her weight dropping from a normal of 110 pounds to 65 pounds, a loss of 45 pounds in a period of 3 months. The hemoglobin dropped to 50 per cent, red blood cells, 3.6 million. Two whole blood transfusions were given and ileostomy was done on November 10, 1938. She improved gradually following this procedure. In January, 1939, an abscess surrounding the splenic



Fig. 5 Barium colon roentgenogram, November, 1930, reveals all demarcated lack of barium contrast limited to the ascending, transverse, and descending colon. Case 6, P.C.



Fig. 6 Barium colon roentgenogram taken July 1931. There is no residual change from condition shown on previous film. Case 6, P.C.

flexure pointed in the left lumbar region and was drained. Her improvement continued for 3 months and she then developed moderately severe exacerbation passing good deal of mucus and blood per rectum. On July 7, 1930, first stage colectomy was done resection being carried to the splenic flexure. Six weeks later on September 1, 1930, the resection was carried to the lower sigmoid. She got along well and gained some weight, but continued to have bloody drainage rectally. Ten months later on November 6, 1930, abdominoperineal resection was done. Now, a year since completion of colectomy she is feeling well. The ileostomy is satisfactorily controlled. Her weight is normal.

The specimen revealed the following: There was marked narrowing of the lumen in two places with thickening of the wall. There were numerous areas of complete ulceration of the mucosa. Some surviving islands of mucosa appeared to be proliferative producing pseudopolyps (Fig. 4). In the remainder the mucous membrane was diffusely hyperemic to hemorrhagic and showed scattered match-head size ulcers with hemorrhagic bases. The microscopic examination revealed evidences of acute and chronic inflammation.

This patient was practically invalided for years before surgical treatment. Ileostomy resulted in some improvement but did not prevent the occurrence of a rather severe exacerbation 3 months later. Her invalidism resulted in a great deal of marital discord as she was greatly opposed to having a permanent ileostomy thinking that this might further estrange her husband. She has been restored to health and happiness.

CASE 5 M.G. female. Illness began in 1913 at age of 20 years. She had severe attacks characterized by abdominal pain, bloody diarrhea, with restlessness, movements daily, vomiting, and fever. She was hospitalized for months during which time no blood transfusion was given. Ten months following the hospital discharge she suffered milder attacks which again necessitated hospitalization. There were moderately severe attacks in February 1915 and February 1914. She was admitted to the Cedars of Lebanon Hospital in August, 1914, on the fifth attack of moderate severity during a period of

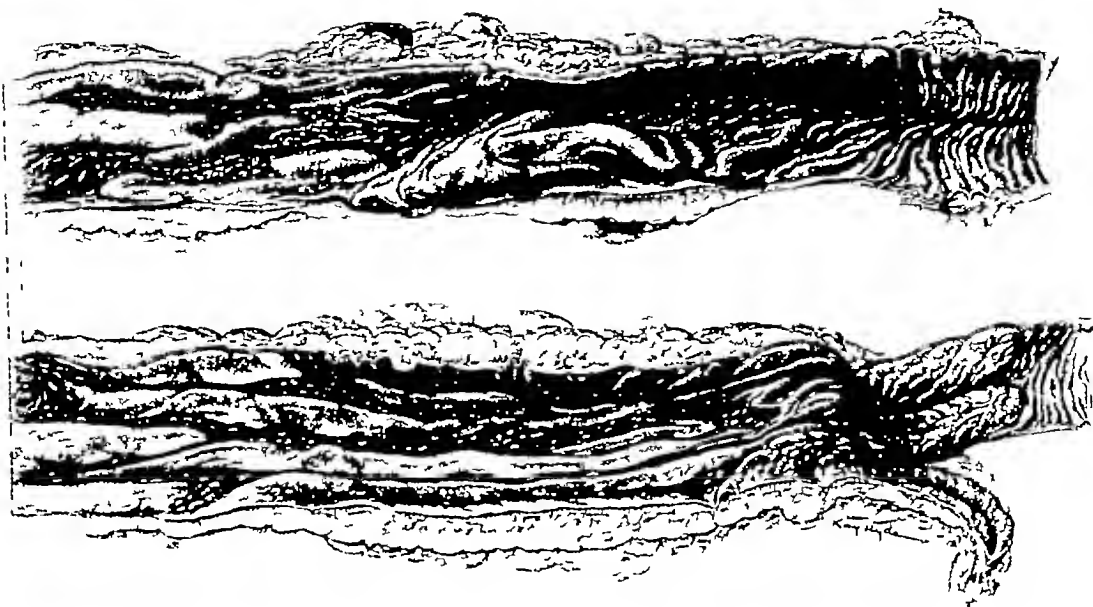


Fig 7 Above, descending colon to line of resection. Below, ascending colon with cecum and attached terminal ileum and appendix reveal the longitudinal furrows which extended practically the full length of the bowel. These furrows were occupied by hemorrhagic membranes which,

when scraped away, revealed the presence of shallow almost continuous erosions. The distal 7 centimeters of bowel appeared to be relatively normal except for the extension of one of the linear furrows clear to the line of resection. Case 6, P C

3 years. After a month's conservative care, an ileostomy was performed in September, 1934. She had no severe exacerbations from this time on, except for a mild one in 1936, when she developed a perirectal abscess which was drained. She gained 30 pounds of weight and felt well, but despite the apparent remission she continued to pass blood and mucus and had lower abdominal cramping pain on frequent occasions.

On September 12, 1939, first stage colectomy was done, resection being carried to the lower sigmoid. Within several days, an unusual local heat wave, with a maximum temperature of 107 degrees F, took place, which lasted for 1 week. The loss of chlorides was increased due to vomiting. Partial dehiscence of the wound occurred. The blood chemistry was corrected and repair was not necessary. Three months later, on December 7, 1939, an abdominoperineal resection was done. It is now 1 year since the completion of the operation. The patient feels very well. She weighs 116 pounds which is about 5 pounds above the previous normal. The ileostomy is satisfactorily controlled.

The specimens showed diffuse marked narrowing of the lumen particularly in the sigmoid where the closed scissors were admitted with difficulty, being about 2 centimeters in diameter at the widest point. There was some thickening of the wall as well as increased firmness. There was atrophy of the mucous

membrane in many areas which appeared to be the result of healed ulcers with scarred bases. The mucosa was represented in a few areas by a few ridges of glistening hemorrhagic rugae, and elsewhere it consisted of hemorrhagic and hyperemic to gray granulation. In the first specimen, 6 centimeters of the bowel showed scattered active ulcers with hemorrhagic borders, the largest being about 1 centimeter in diameter. There were no areas of polyposis or malignancy seen.

Microscopic sections showed virtually complete absence of the mucous membrane which appeared to be replaced by granulation tissue which blended with thickened submucosa. There was connective tissue proliferation in the submucosa and streaking through the muscle fibers. There was infiltration of lymphocytes, plasma cells, and eosinophiles, through all layers, being indicative of chronic inflammatory reaction.

This patient had repeated exacerbations of varying severity for 3 years previous to ileostomy. Following this procedure she appeared to enjoy reasonably good health but continued to pass blood and mucus rectally. Progressive pathological change continued in the bowel despite the ileostomy.



Fig. 3. Section shows acute ulcerative process occurring in the longitudinal furrow at the line of resection. Case 6, P.C. X95.

CASE 6. P.C. female. At 8 years of age this patient had diarrhea which lasted for months. At 6 years, she developed diarrhea following "food poisoning," she thought, consisting of 5 or 6 loose movements daily with no blood, and inconstant cramp-like abdominal pain. She vomited on occasion and lost 5 pounds in 2 weeks. She had ample medical care. The diarrhea persisted for 2 years but her general condition improved slowly. She weighed 74 pounds at 6, and 86 pounds at 8. She suffered moderately acute exacerbation in October, 1930, at the age of 8 years and as admitted to the hospital on October 4. Her immature appearance was noticeable. Menstruation had begun at 4 and had ceased at 6½ year and gain 3 months before her admission. She weighed 80 pounds on admission. She had moderate febrile reaction. Sigmoidoscopic examination revealed an essentially normal mucosa to 10 inches. Barium colon enema (Fig. 5) revealed a rather well demarcated lack of haustration limited to the ascending transverse and descending colon. She had a moderate secondary anemia. A whole blood transfusion and course of neoprontolil were given with some improvement in her condition. She was discharged from the hospital on November 28, 1930. The disease continued only mildly active until

August, 1940, when there was an exacerbation of the symptoms with 8 to 10 movements daily, pain, fever and anemia. She was readmitted to the hospital on August 16, 1940. Sigmoidoscopy revealed some redness of the normal mucosa but no ulcerations to 10 inches. A repeat barium enema (ray taken in July (Fig. 6) had shown no progression in the findings. On September 3 blood transfusion was given, and on September 4, an end-to-side ileosigmoidostomy was done. Examination of the large bowel confirmed the findings which had indicated involvement of the ascending transverse and descending limbs of the colon. These portions of the bowel are thickened and lusterless. There was an abrupt line of demarcation at the sigmoid where the bowel appeared perfectly normal. The anastomosis was carried out 6 to 7 inches below this line of demarcation. Two blood transfusions were given during the week following surgery and the patient reacted well. She had on the average three liquid stools daily. The operative wound healed *per primam*. On October 17 subtotal colectomy was carried out, the bowel being resected from the ileum 14 inches below the line of demarcation in the descending colon. A good many adhesions were encountered in the lower abdomen including fixation of the anastomotic area to the anterior parietal peritoneum. Freeing of the latter resulted in tear into the lumen of the ileum which was repaired. Sulfanilamide therapy was immediately instituted. A blood transfusion was administered following surgery and repeated in 6 days. Within 7 days there was purulent drainage from the wound, followed by fecal drainage and complete dehiscence of the wound. There was copious fluid loss from the wound. She vomited frequently and feeding became a real problem. There was gradual loss of albumin lost in the urine and the serum proteins steadily dropped. Another blood transfusion, the third following surgery, was given. On November 7 on month following the resection, massive hemorrhage from the wound occurred. A tampon had been administered regularly. She was given hyalocast parenterally. Two blood transfusions and 3 cubic centimeters of plasma were also given. The patient died on November 20. Postmortem examination was not permitted.

The surgical specimen revealed a somewhat thickened, narrowed bowel, the serosal surface of which was hyperemic (Fig. 7). The lumen was filled with bright bloody fluid. The mucous membrane was rather smooth and frosted off. There were several irregular but generally longitudinal furrows which extended practically the full length of the colon. These furrows were occupied by hemorrhagic membranes which when scraped away revealed shallow almost confluent erosions. In places there were larger ulcers, the margins of which were composed of overhanging slightly proliferating mucous membrane. This process in the mucous membrane extended to point 7 centimeters from the distal line of resection, the mucous membrane in this latter por-

(Gyathete vitreum, L. Abbott.)

tion of the bowel being more normal in appearance except for the extension of one of the linear furrows in an hemorrhagic erosive manner, clear to the line of resection. Microscopic sections (Fig 8) of the relatively uninvolved portion of bowel revealed mainly acute inflammation with some chronic change, but without involvement of the muscularis or definite ulceration. Sections of the involved area revealed involvement through the whole thickness of the wall.

This case clearly demonstrates the difficulty of ascertaining the extent of involvement by means of the gross, outward appearance of the bowel and x-ray examination. It further demonstrates the importance of proper nutrition and the difficulties one encounters in the postoperative management. We feel that the condition of the bowel contributed to the failure of healing. It now appears that the ileosigmoidostomy was ill-advised, since this was not a case of limited colitis.

CASE 7. C W, male. Illness began in January, 1939, at the age of 39 years, characterized by bloody diarrhea with 8 to 10 movements daily, nausea, vomiting, and diffuse abdominal pain. He lost 60 pounds during the course of 1 month, the previous normal having been about 120 pounds. He was given six blood transfusions. Ileostomy was performed elsewhere in February, 1939. He improved remarkably, regaining 35 pounds during the following 5 months. He was first seen in our out patient department in June, 1939. His weight was 118 pounds and he was having only 3 to 4 rectal passages of pus and mucus daily. He was placed on an ample medical regimen. In February, 1940, he had a mild exacerbation characterized by fever and by abdominal cramps and bloody rectal movements. His weight dropped from 114 pounds to 99 pounds. He was admitted to the hospital on September 27, 1940. Sigmoidoscopic examination revealed active inflammation in the lowermost 8 inches of bowel. He was given sulfathiazol and improved. On November 1, 1940, a subtotal colectomy was performed, resection extending from the ileum to the rectosigmoid. His postoperative reaction was excellent aside from a moderate degree of shock which responded adequately following transfusion. Combined abdominoperineal resection was carried out on December 6, 1940. There was slight postoperative reaction. The abdominal wound is healed and the posterior wound granulating nicely. The ileostomy drainage has noticeably thickened. He now weighs 90 pounds.

The specimens revealed a hemorrhagic appearance of the serosa and roughened hemorrhagic mucosa with numerous bleeding points and many

small ulcerated areas throughout, including the anal canal. The ulcerations involved the full thickness of mucosa and submucosa and a portion of the muscularis. The lumen as a whole was narrowed. Microscopic examination revealed evidences of acute and chronic inflammation.

Ileostomy no doubt was instrumental in saving this man's life. It has not, however, prevented progression of the pathological changes.

CONCLUSION

Surgery finds a place in the treatment of chronic idiopathic ulcerative colitis because of the serious complications of the disease. Total colectomy is logical because it completely eradicates the pathology. It is attended by a reasonable mortality.

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PALE EPITHELIUM IN THE MAMMARY GLAND AND ITS EXPERIMENTAL PRODUCTION IN THE RHESUS MONKEY

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AMONG the vast number of authors who have contributed to the pathology of the human breast a few have interested themselves in certain cells sometimes encountered in the mammary gland remarkable because of their pallor after staining. Opinions concerning the origin, biological significance and practical importance of these atypical cells have been conflicting and almost as numerous as the authors who have written about them. Attempts at clarifying these problems have been based upon the study of pathological human breast tissue obtained either at autopsy or at operation for various types of mammary morbidity.

In a recent study of the effects of intense and prolonged estrogenic stimulation on the rhesus monkey (Hartman, Geschickter and Speert 1941) examination of the mammary glands revealed changes similar to those described and pictured as atypical epithelium or *Masses Zellen*. These observations are recorded here in detail, in the hope that they may throw new light upon an obscure subject.

This atypical epithelium was recognized as a constituent of pathological breasts long before it was specifically mentioned and described in the literature if one may judge from the drawings accompanying some of the early articles on chronic cystic mastitis (Lewer 1858, Sasse, 1897, Roloff 1900, Tietze, 1900). In 1900 Wohlbecker a student of Borst, clearly distinguished between the normal darkly staining cuboidal cells of the mammary gland and the tall pale cells with eccentric nuclei which were seen lining different parts of the same cyst. Paul, in the following year described epithelial changes in chronic cystic mastitis which bore certain points of resemblance. But it was not until 1904 that Borst clearly called attention to these large pale cells lining mammary cysts and named them *atypische Epithelien*. They were further studied by von Saar who in 1907 pointed out their similarity to sweat gland epithelium. Since then they have been variously

referred to in the literature as "*Masses Zellen*", "*Idrosadenoid epithelium*", "*cellules claires*" (Dubet and Mendaro), "*oxyphile Epithelien*" (Prum), "*eosinophils Epithelien*" and "*hells rosige Epithelien*" (Askanazy).

The distinguishing cytological features of these cells are their size and the staining qualities and homogeneity of their cytoplasm. The cells are cuboidal to cylindrical in shape and may under some conditions appear elongated. Their size varies from two to four times that of the normal mammary epithelium. The nuclei are round, vesicular, hypochromatic, and usually centrally located. The abundant pale cytoplasm stains a faint pink with eosin and yellow with van Gieson's stain. It is usually homogeneous and clear, sometimes faintly granular in appearance, and occasionally contains small clear vacuoles.

In describing the epithelial changes in chronic cystic mastitis in 1901 Paul called attention to the cystic arrangement of the "long-celled epithelium" and the intracyclic growth frequently derived from it. The description of atypical epithelium by Borst in 1904 likewise concerned itself with the large pale cells lining mammary cysts. Subsequent studies have emphasized the cystic arrangement of the epithelium in regions where these cells are found. Krompecher (1931) found pale epithelial cysts in 21 of 39 mammary tumors which he studied. Semb (1928) has described cysts lined with pale epithelium as a constant feature in all cases of fibroadenomatous cysts, where they usually occur in large numbers and are more frequent than cysts lined with ordinary mammary epithelium. More recently Dawson (1931) has stated that although the size of the cyst may vary within wide limits, in all cases in which pale epithelium occurs in the breast it lines a definitely cystic structure even the smallest pale structures always appearing larger than normal mammary acini. Cheate and Cutler (1931) have attributed to these pale cells an important rôle in the genesis of mammary cysts, whose formation they described as follows:

"The first change from the normal epithelium of the acinus is the development of cells (cytrophores desquamative

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epithelial hyperplasia) is a slight elongation of the cells. In the next state they become more cuboidal in shape and present a very delicate characteristic appearance. The essential characteristic of these cells is their pallor and they are described by some authors as 'pale cells'. The nuclei are round, hypochromatic, and centrally situated. The cytoplasm is homogeneous and perfectly clear. In the next stage these pallid cells increase in number to form two or three rows from which columns of three or four cells may spring and project into the lumen. It is from the upper cells of these columns as well as from the inner layers lining the acini that desquamation occurs. This process and the collection of fluid distend the acini, forming small cysts. As the condition advances the walls which separate the neighboring acini disappear and a composite cyst is thus formed. These early states result in the later formation of the large cysts in the breast. These cysts are the 'blue-dome cysts' of Bloodgood."

Although occurring predominantly in areas of cystic disease, small cavities lined with pale epithelium have been observed also in association with solid mammary tumors. Thus Krompecher reported 12 cases of pale epithelial cysts occurring with fibroadenomas among his previously mentioned 292 breast tumors, and Semb found 14 such cysts among 100 cases of fibroadenoma.

Pale epithelial cysts are most commonly met with in the fourth and fifth decades, at which ages the various forms of chronic cystic mastitis are most prevalent. However Kudji (1921) has reported such cysts in a 14 year old girl who died of pulmonary tuberculosis before puberty, and Cheatele and Cutler have stated that rarely mammary structures that resemble sweat glands can be found even in the breasts of infants at birth. In adults pale epithelium seems limited to the female in its distribution. Dawson has denied its occurrence in male mammary glands, as has Semb. The latter, however, has described true sweat gland cysts in the male, closely resembling the epithelial lining of fibroadenomatosis in the female breast.

ORIGIN OF PALE EPITHELIUM

The origin of pale epithelial structures in the mammary gland has been accorded various interpretations by different authors. These interpretations may be classified broadly into two groups: first, that the pale structures represent sweat gland epithelium, and second, that they are derived from true mammary epithelium.

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1902, wrote a detailed account of his extensive studies of the sweat glands of mammals and emphasized their relation to mammary development. He believed that tubular glands with the structure of sweat glands were very commonly found in normal breasts as developmental anomalies and that they represented a reversion to a lower type of mammary gland. Similar views concerning the histogenesis of pale epithelium have been expressed by Kuru (1909), who compared it phylogenetically with sweat gland epithelium, and by Krompecher (1913, 1916). The latter author regarded pale cysts as sweat gland cysts and viewed their occurrence in the mammary gland as a manifestation of reversion.

A larger group of authors has vigorously opposed the belief that pale epithelial structures are aberrant sweat glands. The entire subject has been reviewed by Dawson (1932) who concluded that pale epithelium in the breast is derived from normal mammary tissue (ductile or acinar). Her study of sections of mammary glands at various stages of development gave no support to the view that sweat glands are normally included in the breast. Cheatele and Cutler reported similar observations in 1931 and stated that whenever sweat glands resembling mammary structures were encountered they have always been in the extramammary subcutaneous tissue and not in the gland itself. These authors never failed to trace a direct anatomical continuity between the pale structures and the mammary ducts.¹ Dawson observed pale cells and normal mammary epithelium merging directly into each other in the same cystic acinus or duct, and in so doing confirmed the earlier observations of Wohlsecker, Semb, Delbet and Mendaro, and Kudji. This was interpreted as a strong argument for the mammary origin of the pale cells. Krompecher, in 1924, also described both normal and pale epithelium contiguously lining the walls of mammary ducts and cysts, sometimes with almost imperceptible transitions between the two types of tissue. These observations prompted a revision of his previously published views concerning the histogenesis of pale epithelium, which he now regarded as derived from normal mammary structures. Other authors who concluded that the pale epithelium arose from the acini and small ducts of the mature breast include Berka, Prym, and McFarland.

There is general accord among those authors who would derive pale epithelium from true mammary elements, concerning the processes by which the changes occur. Dawson attributes the altera-

¹Ewing (1940) likewise observed glands lined with pale epithelium which emptied into the intralobular lacteal ducts of the normal breast but he regarded the former as sweat glands.

PALE EPITHELIUM IN THE MAMMARY GLAND AND ITS EXPERIMENTAL PRODUCTION IN THE RHESUS MONKEY

HAROLD SPEERT M.D. Baltimore Maryland

AMONG the vast number of authors who have contributed to the pathology of the human breast a few have interested themselves in certain cells sometimes encountered in the mammary gland, remarkable because of their pallor after staining. Opinions concerning the origin, biological significance and practical importance of these atypical cells have been conflicting and almost as numerous as the authors who have written about them. Attempts at clarifying these problems have been based upon the study of pathological human breast tissue obtained either at autopsy or at operation for various types of mammary morbidity.

In a recent study of the effects of intense and prolonged estrogenic stimulation on the rhesus monkey (Hartman, Geschickter and Speert 1954) examination of the mammary glands revealed changes similar to those described and pictured as atypical epithelium or *Blasse Zellen*. These observations are recorded here in detail, in the hope that they may throw new light upon an obscure subject.

This atypical epithelium was recognized as a constituent of pathological breasts long before it was specifically mentioned and described in the literature if one may judge from the drawings accompanying some of the early articles on chronic cystic mastitis (Lewer 888 Same 1897 Roloff 1900 Tietze 1900). In 1900 Wohlbecker a student of Borst clearly distinguished between the normal darkly staining cuboidal cells of the mammary gland and the tall pale cells with circular nuclei which were seen lining different parts of the same cyst. Paul, in the following year described epithelial changes in chronic cystic mastitis which bore certain points of resemblance. But it was not until 1904 that Borst clearly called attention to these large pale cells lining mammary cysts and named them *atypische Epithelien*. They were further studied by von Saar who in 1907 pointed out their similarity to sweat gland epithelium. Since then they have been variously

referred to in the literature as *blasse Zellen*, *fibroadenoid epithelium*, *cellules claires* (Delbet and Mendarm), *atypical Epithelium* (Prym), *clear atypical Epithelien* and *belle rosige Epithelien* (Askanazy).

The distinguishing cytological features of these cells are their size and the staining qualities and homogeneity of their cytoplasm. The cells are cuboidal to cylindrical in shape and may under some conditions appear elongated. Their size varies from two to four times that of the normal mammary epithelium. The nuclei are round, vesicular, hypochromatic, and usually centrally located. The abundant pale cytoplasm stains a faint pink with eosin and yellow with van Gieson's stain. It is usually homogeneous and clear, some times faintly granular in appearance, and occasionally contains small clear vacuoles.

In describing the epithelial changes in chronic cystic mastitis in 1907 Paul called attention to the cystic arrangement of the "long-celled epithelium" and the intracystic growth frequently derived from it. The description of atypical epithelium by Borst in 1904 likewise concerned itself with the large pale cells lining mammary cysts. Subsequent studies have emphasized the cystic arrangement of the epithelium in regions where these cells are found. Krompecher (1913) found pale epithelial cysts in 21 of 292 mammary tumors which he studied. Semb (1923) has described cysts lined with pale epithelium as a constant feature in all cases of fibroadenomatous cysts, where they usually occur in large numbers and are more frequent than cysts lined with ordinary mammary epithelium. More recently Dawson (1932) has stated that although the size of the cyst may vary within wide limits, in all cases in which pale epithelium occurs in the breast it lines a definitely cystic structure, even the smallest pale structures always appearing larger than normal mammary acini. Cheate and Cutler (1933) have attributed to these pale cells an important rôle in the genesis of mammary cysts, whose formation they described as follows:

"The first change from the normal epithelium of the acini into the desquamated state (cytokeratin desquamation)

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epithelial hyperplasia) is a slight elongation of the cells. In the next state they become more cuboidal in shape and present a very delicate characteristic appearance. The essential characteristic of these cells is their pallor and they are described by some authors as 'pale cells'. The nuclei are round, hypochromatic, and centrally situated. The cytoplasm is homogeneous and perfectly clear. In the next stage these pallid cells increase in number to form two or three rows from which columns of three or four cells may spring and project into the lumen. It is from the upper cells of these columns as well as from the inner layers lining the acini that desquamation occurs. This process and the collection of fluid distend the acini, forming small cysts. As the condition advances the walls which separate the neighboring acini disappear and a composite cyst is thus formed. These early states result in the later formation of the large cysts in the breast. These cysts are the 'blue-dome cysts' of Bloodgood.²

Although occurring predominantly in areas of cystic disease, small cavities lined with pale epithelium have been observed also in association with solid mammary tumors. Thus Krompecher reported 12 cases of pale epithelial cysts occurring with fibroadenomas among his previously mentioned 292 breast tumors, and Semb found 14 such cysts among 100 cases of fibroadenoma.

Pale epithelial cysts are most commonly met with in the fourth and fifth decades, at which ages the various forms of chronic cystic mastitis are most prevalent. However Kudjı (1921) has reported such cysts in a 14 year old girl who died of pulmonary tuberculosis before puberty, and Cheate and Cutler have stated that rarely mammary structures that resemble sweat glands can be found even in the breasts of infants at birth. In adults pale epithelium seems limited to the female in its distribution. Dawson has denied its occurrence in male mammary glands, as has Semb. The latter, however, has described true sweat gland cysts in the male, closely resembling the epithelial lining of fibroadenomatosis in the female breast.

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tions in morphology and staining affinities to degenerative changes which occur following antecedent stimulation of the epithelium. She found pale epithelial cysts predominantly associated with the glandular involution of the menopause. Thus she regarded the pale change as evidence of receding epithelial activity supervening on the proliferative states of the normal epithelium. Berkha had expressed a somewhat similar view in 1912. This author apparently found pale epithelium only in the breasts of women who had borne children, and considered such tissue a result of incomplete involution after pregnancy. McFarland regarded pale epithelial cysts as residual lactation acini. The mechanism by which the pale change occurs has been explained by Kodjji as a temporary increase in the blood supply with resultant growth, followed by a secondary decrease in blood supply caused by hormonal withdrawal with resultant degeneration of the parenchyma.

A modified interpretation of pale epithelium has been advanced by Thiele. He regarded this tissue as a special degeneration form of the mammary elements, differentiated from the normal cells by virtue of its greater growth energy (papillary formations) secretory activity (vacuole formation) and shorter life span (no large masses of cells despite rapid multiplication desquamates into cysts).

RELATION TO CANCER

The greatest interest in the nature of pale epithelium has centered about the long waged controversy concerning its possible relation to carcinogenesis in the mammary gland. Opinion has been divided into two main groups which have championed opposite views: that pale epithelium indicates a change either of early malignant neoplasia or with a definite possibility of subsequent transformation into cancer; and that the pale change is essentially degenerative, rather than neoplastic, with little or no possibility of subsequent malignant tumor.

The earliest claims for the carcinomatous nature of the large atypical pale cells lining mammary cysts are found in the writings of Borst in 1904. Berkha, Krompacher, Askanazy and Fraser in subsequent publications, have regarded pale epithelium as a precancerous alteration of mammary epithelium. In the series of breast tumors reported by Krompacher pale epithelium was observed in 9 cases of cancer. Seub found pale epithelium in 35 of 111 cases of cancer of the mammary gland. Dawson succeeded in demonstrating pale structures in 6 of 20 breasts containing malignant tumors. These observations

were interpreted as corroborative evidence of the pathogenetic relationship between pale epithelium and mammary neoplasms.

Ewing has stated that 25 per cent of mammary cancers are of sweat gland origin, and Lee, Pack, and Scharnagel have described 81 so called "sweat gland cancers from Ewing's laboratory. Their findings, while not in themselves indicating a specific malignant tendency of pale epithelium, have at least shown this tissue to be susceptible of carcinomatous change. Chentle and Cutler also agree that these cells are the frequent site of origin of cancer of the breast, in agreement with Cohnheim's theory of malignant change from misplaced cell rests. Dawson on the other hand, has denied the existence of true sweat gland carcinomas of the breast.

Attention has been called to the morphological similarity between atypical pale epithelium and Paget cells. Semb found pale cells present in the excretory ducts and milk ducts under the nipple and in 6 cases of Paget's disease atypical pale epithelium was found in the mammary tissue of all. He was thus led to state in 1928 that "from my investigations I assume that the proliferation in Paget's disease primarily begins with the growth of the atypical pale epithelium in the large milk ducts under the nipple. From here the proliferation as a constant rule extends to the epidermis of the nipple, with formation of the cancer tumor."

Other authors have denied, with equal emphasis, that pale epithelium is a sign of malignant new-growth or that it is in any way related to carcinogenesis. Mueller found areas of early cancer in the vicinity of the pale epithelial cysts in his case but denied a relationship between the two. Kott interpreted the presence of pale epithelium in the mammary glands of children as evidence against cancer. The absence of ulcers and of invasiveness were pointed out by Kodjji as additional features of pale epithelium suggesting its benignancy. Thiele and von Saar among others, likewise denied any malignant tendencies of pale epithelium.

Semb has clearly distinguished between the significance of the pale epithelium seen in mammary fibroadenomas and that occurring in cases of fibroadenomatosis cystica. He observed small cysts lined with pale epithelium in 14 of 100 cases of the former but felt that no importance for the tumor formation could be ascribed to this epithelium since it occurred in too scant quantities in the separate tumors. Furthermore since fibroadenomas seldom go over into cancer neither could this pale epithelium be regarded as a sign

of "malign degeneration" in the fibroadenoma. In the cases of fibroadenomatosis cystica, on the other hand, small cystic cavities lined with pale epithelium were observed, with atypical changes and penetration of the basement membrane and distinct infiltrating growth. These changes were found in 9 of 24 cases. Semb, therefore, concluded that in these cases pale epithelium served as the starting point for cancer development.

ANIMAL STUDIES

Study of the published opinions of the aforementioned authors does not permit of definite conclusions concerning the nature of pale epithelium in the mammary gland, nor its biological or pathological significance. Because of the lack of agreement resulting from studies based on human pathological material, it is desirable to obtain evidence from other species resulting from an experimental approach to the problem.

Observations on the occurrence of "pale epithelium" in the mammary glands of animals other than the human are very scant. Fifer (1934) described cysts with hyperplastic and metaplastic epithelium (possibly pale) in the breasts of rabbits during the postlactation interval but not during periods of functional activity (estrus, pregnancy, pseudopregnancy, and lactation). These findings are in agreement with the concept of pale epithelium advanced by Dawson, Berka, and by McFarland, namely, that the pale change occurs as a result of receding epithelial activity following upon antecedent stimulation. Fifer observed similar pale changes, however, in the breasts of males and virgin females also.

In 1936 Macdonald reported areas of intracanalicular hyperplasia in the mammary glands of castrated rabbits receiving 25 to 200 rat units of estrogenic hormone daily. Some areas of the hyperplastic growth resembled pale epithelium. The following year similar changes occurring in mammary cysts were reported by Herold and Effkeman, who injected normal and castrated male and castrated female rats for periods up to 3 months with amounts of estrogens ranging between 50 and 1000 international units daily. However, such changes were rarely produced in the glands of intact females which were similarly treated.

PERSONAL OBSERVATIONS

In collaboration with Dr. Carl G. Hartman and Dr. Charles F. Geschickter, the writer has recently made a study of the effects of the long term treatment of rhesus monkeys with very large amounts of estrogenic hormones. These ob-

servations have already been reported briefly¹ and will be described in detail elsewhere.

The animals were treated by subcutaneous implantations of two estrone pellets weekly, weighing 3 milligrams each, and subcutaneous injections of 10,000 international units of amniotin (Squibb) every other day. Studies of the mammary glands include 32 specimens obtained from 15 females ranging in weight from 2,180 to 3,970 grams. Eight of the animals were surgically castrated immediately before the institution of estrogenic treatment, in the 7 remaining the ovaries were left intact. The specimens represent material obtained at autopsy or by repeated biopsies after periods of treatment ranging from 2 to 29 months.

Soon after the onset of treatment a marked hyperplasia with resultant stratification of the duct epithelium occurred. At the end of about a month the ducts began to dilate as the epithelial hyperplasia began to wane, and budding of the duct system occurred. Within 2 months evidence of early lobule formation was detectable. Development of the gland progressed thereafter in an orderly fashion to complete unfolding of the lobule-alveolar system. These developmental changes have been observed in the same animal by repeated biopsies at different stages of treatment.

This pattern of mammary development in response to estrogenic stimulation was found to occur with fair uniformity in all the animals, and appeared not to be dependent upon their weight or the presence or absence of the ovaries. On the other hand, the pale changes to be described occurred predominantly among the castrates. Of the 5 animals in which pale epithelium was observed 4 were castrates, an incidence of 50 per cent among this group, whereas pale epithelium was found only once in the mammary glands of the 7 noncastrated monkeys, an incidence of only 14 per cent. This finding is in agreement with the observations of Herold and Effkeman, who failed to detect pale epithelium among their intact estrogen treated female rats, whereas the mammary glands of the castrates developed cysts lined with pale epithelium.

Concurrently with the orderly development of the mammary gland just described, the pale cells made their appearance. They were seen at various stages after the 10th week of estrogenic treatment. In contrast to the cystic arrangement of the pale cells which has been described in pathological human mammary glands, the pale epithelium in our experimental monkey specimens appeared as small islets of these atypical cells usually compactly arranged, although there was occa-



Fig. G 5—castrata. Mammary gland biopsy specimen after 14 months of estrogenic treatment. Islet of pale epithelium adjacent dilated duct, center. Hematoxylin and eosin, X60.



Fig. G 6—Higher magnification of same specimen as shown in Figure G 5, showing pale epithelial cells in contrast to normal mammary epithelium, X145.

sionally a suggestion of acinus formation. These groups of cells were irregularly spaced among the normal mammary lobules, with which they formed a sharp contrast (Figs 1 to 3). Less frequently the pale cells were seen in the linings of the mammary ducts, merging and contrasting with the normal mammary epithelium (Fig. 3).

The cells were two to three times as large as the normal mammary cells, cuboidal or polygonal in shape. The nuclei were large, round, vesicular, hypochromatic, and contained prominent nucleoli. They were usually centrally but occasion-

ally basally located. The cytoplasm was very pale, faintly eosinophilic and appeared perfectly clear at low power magnification. At higher magnification the cytoplasm was found to be very finely granular, and in some instances contained vacuoles of varying size.

ANALYSIS OF STUDY

The metaplastic change in the mammary gland represented by the appearance of pale epithelium is interpreted as a specific response to intensive estrogenic stimulation. Of 474 specimens obtained from the breasts of 304 male and female rhesus monkeys under all sorts of physiological and experimental conditions, pale epithelium was found in none outside of the series here mentioned. The occurrence of this atypical epithelium in the glands of only those monkeys which had been treated with large amounts of estrogenic agents strongly points to this hormone as the causative agent. Furthermore, since 4 of the 5 cases manifesting pale epithelium were among the castrated animals (which group constituted only a small proportion of the monkeys in the Carnegie colony) it is suggested that the absence of the ovaries may have been an important prerequisite factor for the attainment of this change.

In explanation of the pathological changes noted in their estrogen treated castrated rats and the failure of those with intact ovaries to develop similar mastopathies, Herold and Effleman have stressed the importance of the corpus luteum. Functionally intact tissue persisted in the ovaries in response to estrogenic stimulation, a phenomenon which was first demonstrated in the rabbit (Allen



Fig. G 24—castrata. Mammary gland biopsy specimen after 14 months of estrogenic treatment. Not intimate relation between pale epithelium and normal acinar cells, and contrast between pale and normal cells in duct linings. Hematoxylin and eosin, X60.

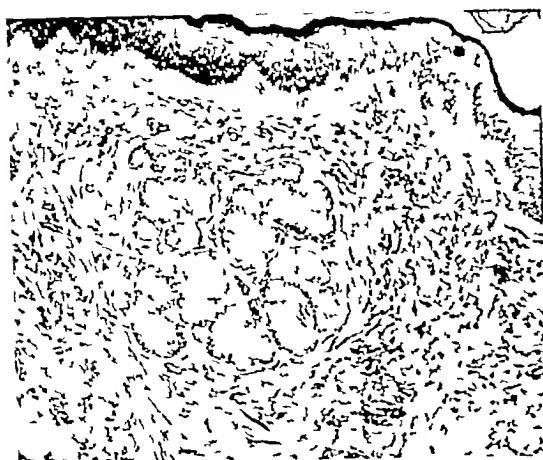


Fig 4. No 140—castrate Photomicrograph showing the marked hyperplasia of the sebaceous gland after the animal had received 6 weeks of estrogenic treatment. Hematoxylin and eosin, $\times 60$



Fig 5. No 134—castrate Sweat gland adenoma (upper right) after 6 weeks of estrogenic treatment, shown in relation to normal mammary lobule and hyperplastic ducts. Hematoxylin and eosin, $\times 37$

and Heckel, 1936) The mammary glands of the intact rats were thus regarded as being under the balanced influence of estrogen and progesterone. In the castrates, on the other hand, the estrogens were allowed to exercise an unopposed effect upon the mammary glands. It is possible that estrogens stimulate the monkey's ovary, either directly or through the mediation of the pituitary, to produce progesterone or some other hormone, which may help prevent the appearance of the pale change in the macaque's breast. Since little is known concerning the effects of estrogens on the structure of the monkey's ovary, and even less concerning the effects upon ovarian function, however, this suggestion is to be regarded as purely speculative.

The changes which occur in the anterior pituitary following castration provide an alternative explanation for the high incidence of pale epithelium among the castrates in contrast to the noncastrated animals. After bilateral ovariectomy, profound alterations occur in the functioning of this gland. In the human, for example, increased quantities of pituitary gonadotropic hormone appear in the blood and urine. Specific cytological alterations occur at this time in the pituitaries of several species, including the rhesus monkey (Severinghaus, 1939). During the past few years a large body of suggestive evidence has accumulated attributing to the anterior pituitary specific mammogenic activity. Perverted pituitary function, in conjunction with the estrogens administered in the present experiments, may thus be responsible for the changes observed in the mammary glands.

An additional channel through which altered pituitary function may affect the mammary glands involves the mediation of the adrenals. The adrenal cortex produces estrogens, androgens, and other steroid substances which are effective stimulators of mammary growth (Speert, 1940). Yet adrenal function is, in turn, under control of the anterior pituitary. Thus under conditions of pituitary hyperactivity, augmented secretion by the adrenal cortex may ensue with resultant effects upon the mammary gland.

In addition to the pale changes described, two other somewhat similar alterations have been observed in the mammary glands of castrated monkeys receiving smaller amounts of estrogens. One occurred following the daily administration of 100 rat units of amniotin (Squibb) for a period of 6 weeks. Examination of the breast at the end of this period revealed a marked hyperplasia of the pale staining sebaceous apparatus in the subcutaneous tissue (Fig 4). This change is probably comparable to the condition which Florentin and Binder (1939) succeeded in producing in the guinea pig mammary gland by the injection of 55,000 international units of estrogenic hormone over a period of 6 weeks, and referred to by them as "sebaceous metaplasia."

The second pathological change likewise was found after a 6 weeks' period of estrogenic stimulation, this animal having been treated daily with 5,000 rat units of amniotin. A small adenoma about twice the size of the average mammary lobule and consisting of typical sweat gland tissue was found embedded in the substance of the mam-

mmary gland. It is shown in Figure 3 in relation to a normal mammary lobule and two hyperplastic ducts. The relative pallor of the sweat gland epithelium affords a definite striking contrast to the more darkly staining cells of the mammary gland.

Sebaceous hyperplasia and sweat gland adenomas were not found in any other mammary glands of the large control series previously mentioned. Yet the appearance in the breasts of these epithelial overgrowths, of sebaceous gland cells on the one hand and of sweat gland cells on the other, makes possible a morphological comparison of these cells with those comprising the pale epithelium. It becomes immediately apparent that we are dealing with three distinct cell types, the only common characteristic being that the cytoplasm of each stains less intensely than that of the normal mammary epithelium.

There is little cytological similarity between the pale epithelium¹ and that of the sweat glands in the monkey breast. The cells of the latter are smaller, the cytoplasm more eosinophilic and the nuclei smaller and more darkly staining. More closely on the other hand, do the "pale cells" resemble the cells of the sebaceous glands, although the latter too have smaller and more darkly staining nuclei.

We are thus led to the conclusion that the pale cells represent variants of the normal mammary gland cells. The characteristic appearance of the former results from the metaplastic change stimulated by the continuous and unopposed action of very large amounts of estrogens. The view that these cells arise from the mammary epithelium is strengthened not only by their morphological contrast with the other possible precursors, but also by their intimate relation to the normal elements comprising the mammary lobules and ducts (Fig. 3).

It is by no means certain that the many published papers dealing with atypical or pale epithelium have concerned themselves with the same cell type, for the illustrations accompanying the articles have been neither sufficiently numerous nor clear. Conclusions drawn from the present studies are, therefore, of limited applicability to the problems of pale epithelium as they exist in the literature. Yet it seems safe to conclude that the present experimentally produced pale epithelium is comparable to at least some of the lesions described in the human mammary gland, so closely do our specimens resemble some of the published illustrations of this condition (cf. Deibel and Mendaro, Fig. 7, p. 22). The common failure of ovulation to occur in premenopausal women

may give rise to a condition in the human comparable to that of our experiments, namely the continued unopposed action of high estrogen levels.

Carcinoma of the mammary gland has been produced in susceptible strains of mice by several investigators by means of various estrogenic hormones (see review by Gardner 1939). Geschickter had recently succeeded in inducing mammary cancer in rats also after intensive estrogenic treatment. Although the amounts of estrogens required for the production of malignant changes in the breasts of rodents are proportionately many times greater than the doses ordinarily used clinically in the treatment of patients, these studies have naturally brought into question the complete safety of prolonged estrogenic therapy in the human. Indeed isolated case reports (Allaben and Owen, 1939; Auchincloss and Hsaugen, 1940; Parsons and McCall 1941) have suggested a possible carcinogenic action of estrogens on the human breast.

The present experiments were originally begun by Dr. Geschickter with the view of determining the possibility of producing cancer of the mammary gland in the rhesus monkey with estrogenic hormones. All the mammary specimens are therefore studied in great detail and pathological changes carefully sought. Aside from the transitory hyperplasia and dilatation of the ducts, the appearance of pale epithelium was the only pathological change noted in the breasts. The pale cells were of uniform appearance, gave no evidence of invasiveness, and no mitotic figures were seen among them. Among the animals that came to autopsy there was no suggestion of metastases. Thus no support can be offered for the view that pale epithelium, at least as it is observed in the mammary gland of the monkey, is in itself a malignant tumor type of epithelium or that it has any malignant tumor potentialities.

SUMMARY

The literature on "pale epithelium" in the human mammary gland has been reviewed. Changes resembling this condition have been produced in the breasts of rhesus monkeys by the administration of very large amounts of estrogenic hormones. These changes are observed predominantly among the castrated animals. Evidence indicates that pale epithelium represents a metaplastic alteration of normal mammary gland cells, but no support is offered for the belief that this change in the cells has a significance for the subsequent development of carcinoma of the breast.

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PERSISTENCE OF TUMOR AFTER PREOPERATIVE RADIUM TREATMENT FOR CANCER OF THE CORPUS UTERI

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RADIATION therapy has come to occupy a position of great value in the treatment of carcinoma of the body of the uterus. Aside from the fact that this is the only effective treatment available for patients who are inoperable because of local extent of the growth or for constitutional reasons, intrauterine radium therapy with or without external irradiation with roentgen rays, has been accepted in most large centers in this country and in Europe as an important preoperative measure. However, the French cancer therapists in general do not subscribe to this view using radium and roentgen rays for palliation only of endometrial cancer. German radiologists have treated carcinoma of the uterine body since 1911 (9) and by 1915 this method was in use at other European clinics and in America.

Originally many cancer therapists felt that irradiation of endometrial cancer was unwise since surgical methods gave quite a satisfactory number of cures, and there was a widespread opinion that adenocarcinoma was not radiosensitive. However, because many women with this type of cancer were inoperable some form of radiation therapy was used, and it soon became apparent that this type of treatment would effect a fair percentage of cures.

In 1917 Heyman published a report from the Radiumhemmet in Stockholm which tended to give radiation as good a standing as surgery in the treatment of cancer of the uterine body (5). He first tabulated the reports of 38 patients treated by operation alone in 6 different European clinics, with an average 5 year cure of 4.3 per cent. Counting only the strictly operable cases the recovery was 58.8 per cent. He then reported 46 patients treated at the Radiumhemmet with intrauterine radium alone, with a recovery rate of 43.5 per cent. Twenty five of these patients were technically and clinically operable and of

these, 15 or 60 per cent recovered after radium therapy.

By 1933, Hurdon and Chambers were able to collect reports from Stockholm, Berlin, Munich, New York (Memorial Hospital) and Baltimore (Howard Kelly Hospital) totaling 359 operable cases of endometrial cancer treated by radiation methods. One hundred and ninety-six patients survived 5 years, 54.5 per cent, and of 381 inoperable cases, 42 or 11 per cent, lived 5 years.

Heyman, in reporting the technique of treating corpus carcinoma at the Radiumhemmet in 1935 (6) stated that he filled the uterus with small containers of radium, giving 2600-4000 milligram hours in treatments, plus one vaginal treatment to prevent metastasis in this location. If symptoms did not disappear or if new symptoms appeared such as bleeding, discharge, or an increase in size of the uterus, a total hysterectomy was done. In this paper he reported that in 48.7 per cent of 56 cases, patients were cured by radium therapy.

A year later Heyman (4) summarized the results of treatment in carcinoma of the body of the uterus for a 16 year period and showed that in both the technically and clinically operable groups the survival rate was better in those who had a hysterectomy than in those who were not operated on. He therefore advised that this operation be done on all patients who were suitable risks.

Irradiation, chiefly by intrauterine radium, followed in 4 to 8 weeks by panhysterectomy and salpingo-oophorectomy has been recommended in many recent publications as the treatment of choice for cancer of the uterine body (1,2,3,4, 5). Miller agrees that a combination of irradiation and surgery is better than operative treatment alone but he believes that preoperative roentgen treatment is more efficacious than intrauterine radium and uses the latter only for obese patients and those who are inoperable. He reports 90 per cent of 54 patients as surviving 5 years after irradiation followed by surgery or 82 per cent if corrected for noncancer deaths. Healy and Brown reported 75 per cent of 8 patients well and free of cancer 2.5 years after a dosage of 3000-4000 millicurie hours of radon followed by panhysterectomy 1 to 4 months later.

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We are indebted to the chief of the division of gynecology at the Palmer Memorial Hospital and Collis P. Huntington Memorial Hospital, Dr. George A. Lehard, Jr. for permission to refer to the clinical data used. Dr. Joe V. Meyer will report later on the clinical aspects of the cases from the Pundlich State Hospital for Cancer.

Masson and Gregg have reported that among 42 technically operable patients treated by irradiation alone, they obtained 50.5 per cent 5 year survival. They also stated "In our series the difference in five and ten-year cure after operation with and without irradiation is too small to be of significance."

The method of treating uterine corpus carcinoma at the Palmer Memorial Hospital has usually been an intrauterine radon treatment, followed by hysterectomy in the operable cases after an interval of 6 to 10 weeks. Dr. Meigs will report later on the type of treatment used at the Pondville Hospital. Because of the frequent presence of active carcinoma in these irradiated uteri when removed at operation, it occurred to us to check over the survival of tumor tissue in the specimens received in the pathological laboratories. In all, 46 cases are included. The various dosages of radon which were used are shown in Table I.

In all cases the diagnosis was made by microscopic examination of curettings prior to the insertion of radon. The latter was applied by means of various types of single applicators, of a length conforming to that of the uterocervical canal. In only 4 cases was there more than one application. Only those cases have been included in which the hysterectomy and salpingo-oophorectomy were done 6 weeks or more after the irradiation, so that there was adequate time for the full effect of the irradiation to become manifest. In one case the interval was 1 year because the patient was a poor operative risk due to obesity, but later lost weight. The longest interval was 2 years, as the patient refused operation and later changed her mind. Three patients had roentgen ray treatment in addition to the local radon, the reason in 2 of them being that they were originally diagnosed as carcinomas of the cervix.

Of the 46 cases summarized in Table I, it will be seen that only 5 uteri were free of carcinoma at the time of hysterectomy, 11 per cent. It is interesting to note that this figure of 11 per cent corresponds very closely to the average 5-year survival of 381 inoperable and irradiated cases reported by Hurdon and Chambers.

In our cases there was no special effort to find carcinoma in any of the uteri. Routine sections taken from what appeared grossly to be representative areas were examined and reported as showing carcinoma or no carcinoma. No further sections were made in any case which failed to show cancer in the first slides examined. The amount of tumor which was present varied from large amounts to scattered small foci of cancer in the

TABLE I—DOSAGE USED IN PREOPERATIVE RADIUM TREATMENT OF CARCINOMA OF CORPUS UTERI

Dosage in mc-hrs	Number treated	Uteri free of carcinoma when removed
1700-2000	1	1
2000-2500	6	1
2500-3000	6	0
3000-3500	18	1
3500-4000	13	2
4000-4500	2	0
Total	46	5

myometrium which would obviously have been sources of recurrence had the uterus been left *in situ*. In a few cases the cancer showed no detrimental effect from a radon dosage that clearly had damaged the myometrium and its vessels.

There is but little to be found in the literature on the persistence of carcinoma in preoperatively irradiated uteri. Arneson states that "Six patients received more than 3000 mg-hrs of radium. In 4 of these no tumor could be demonstrated in specimens taken 2 to 8 months after the intrauterine treatment. Active disease was found in every instance if the dose had been less than 3000 mg-hrs." But only 4 cases were included in the latter group. Healy and Brown studied 75 uteri after operation and said that "of six patients who received roentgen rays only, all showed residual carcinoma. In twenty-four cases in which the intracavitary radon dosage varied from 1200 to 2700 mc-hrs, complete regression occurred in only 12 per cent. In twenty-five cases in which the dosage was from 3000 to 3300 mc-hrs, there was complete disappearance of carcinoma in 52 per cent, while in twenty patients receiving 3400 to 4000 mc-hrs, 60 per cent showed no residual carcinoma." Thus, 40 per cent of their patients receiving the largest dosage showed residual carcinoma and this was an important factor in their conclusion that the uterus should be removed in all operable cases. In the discussion of this article, Dr. J. A. Corscaden said that of 21 uteri removed at his clinic following irradiation for carcinoma of the corpus, 8 were free of cancer.

There is no longer the unanimity of opinion about the merits of using intrauterine radium as a preoperative measure in the clearly operable patients which apparently existed a few years back. Miller states that the problem of adequately treating an endometrial cancer by radium has not been solved by multiple applications or by multiple applicators. He gives this as an important reason for preferring preoperative roentgen

TABLE II A--SUMMARY OF CASES

No. Patient, Age	History	Diagnosis on surgery	Radiation damage to the ovary	Interval between radiation and operation	Operation	Laboratory report	Result
E. S. 52	Varied bleeding for years	Adenocarcinoma	70%	8 mos	Partial hysterectomy and bilateral salpingo-oophorectomy	Uterus 3 by 3 by 1 cm. Endometrium negative, radiation reaction of myometrium. Hydrosalpinx, left. Chronic cervicitis	Well yrs. later
A. S. 66	Bleeding for 3-7 yrs	Adenocarcinoma	100% plus about 1/2 each of 4 pelvic ports	2 wks	Same	Uterus 3 by 3 by 1 cm. Cervix normal. No radiation reaction. No evidence of metastasis.	Recovered from radiation; no later for metastasis
V. C. 64	Bleeding for 5 yrs	Adenocarcinoma	32	6 wks	Same	Uterus not measured, endometrium thickened to 1 cm. No evidence of metastasis.	Well 10 yrs. later
A. W. 52	Discharge and bleeding for 37	Adenocarcinoma	32%	10 ks	Same	Uterus normal size. Endometrium greatly negative except for one slightly enlarged area. Microscopic examination, negative and moderate reaction of uterus, negative tubes and ovaries	Well yrs. later
E. C. 58	Irregular bleeding for 3 yrs	Adenocarcinoma	100%	1 st mos	Same	Uterus 3 by 3 cm. Radiation reaction and atrophy of endometrium. No evidence of metastasis.	Well 6 yrs. later
M. W. 51	Irregular bleeding during menstruation	Adenocarcinoma	20-40	10	Same	Uterus not measured. Cervix normal. No evidence of metastasis.	Well yrs. later
C. L. 54	Menstruation for years	Adenocarcinoma	10%	6 mos	Same	Uterus 3 by 3 by 1 cm. Adenocarcinoma with moderate reaction, moderate endometrium, negative ovaries	Isolated this later by clinical means of metastasis. Free metastasis
M. A. 54	Bleeding for yrs	Adenocarcinoma	10%	1 mos	Same	Uterus 3 by 3 by 1 cm. Adenocarcinoma with radiation reaction of uterus, negative tubes and ovaries	Dead not later
M. H. 61	Bleeding for mos	Adenocarcinoma	100%	1 mos	Same	Uterus 3 by 3 by 1 cm. Adenocarcinoma with radiation reaction	Dead on 10th postoperative day. Tubes perforated and ruptured
M. A. 50	Bleeding yrs	Adenocarcinoma	30%	6 ks	Same	Uterus 3 by 3 by 1 cm. Adenocarcinoma with radiation reaction of uterus and superficial parts of vagina	Well mos. later
F. S. 56	Bleeding during menstruation	Adenocarcinoma	77%	8 wks	Same	Uterus 3 by 3 by 1 cm. Adenocarcinoma with radiation reaction. Tubes and ovaries negative	
M. K. 45	Bleeding for mos	Adenocarcinoma	100%	6 ks	Same	Uterus 3 by 3 by 1 cm. Atrophy of endometrium with moderate reaction of endometrium and early radiation reaction. Negative tubes and ovaries	
M. T. 47	Bleeding for mos	Adenocarcinoma	30%	8 wks	Same	Radiation reaction of endometrium with some enlargement. Uterus showing moderate reaction	all of mos. later

TABLE II B—SUMMARY OF CASES OF PATIENTS RECEIVING PREOPERATIVE RADIATION THERAPY AT PONDVILLE HOSPITAL

No Patient Age	Diagnosis on curettings	Laboratory report	No Patient Age	Diagnosis on curettings	Laboratory report
1 P C 58	Carcinoma with moderate radiation reaction	Uterus 8 by 6 by 4 cm Adenocarcinoma present	18 E H 55	Adenocarcinoma	Adenocarcinoma with invasion of myometrium Leiomyoma negative tubes and ovaries
2 A W 68	Adenocarcinoma	Uterus 7 by 5 by 2.2 cm Adenocarcinoma with radiation reaction Tubes and ovaries negative	19 L H 69	Adenoacanthoma	Radiation reaction of uterus with scattered foci of carcinoma
3 I B 64	Adenoacanthoma	Uterus small not measured Carcinoma insufficient for diagnosis	20 M B 68	Adenocarcinoma	Adenocarcinoma with implantation on appendix
4 F D 59	Adenocarcinoma	Uterus 9 by 4.5 by 3 cm Adenocarcinoma with radiation reaction	21 F N 52	Adenoacanthoma	Adenoacanthoma with invasion of myometrium
5 L C 50	Adenocarcinoma	Uterus 9 by 8 by 4.5 cm Grossly 3 cm tumor nodule in fundus Adenocarcinoma dermoid cyst of ovary	22 M A 32	Adenocarcinoma	Uterus 11 by 7 cm Adenocarcinoma
6 M B 56	Adenocarcinoma	Uterus 7 by 4 cm Radiation reaction with a focus of tumor in myometrium	23 M P 63	Carcinoma simplex	Uterus 8 by 6 by 3 cm Carcinoma simplex diffuse invasion of myometrium radiation reaction and necrosis Biopsy of recurrence in pelvis showed carcinoma 2 months later
7 J C 55	Adenoacanthoma	Uterus 9.5 by 6.5 cm Radiation reaction with no tumor Metastases to tubes and ovaries	24 M C 58	Adenocarcinoma	Uterus 10 by 10 by 7 cm Several large leiomyomas Adenocarcinoma with slight radiation reaction Papillary adenocystoma of right ovary
8 B G 32	Adenocarcinoma	Uterus 9 by 6 by 4.5 cm Radiation reaction of uterus and chronic cervicitis	25 H F 56	Adenoacanthoma	Uterus 8 by 5 by 4.5 cm Radiation reaction of endometrium and myometrium with foci of adenoacanthoma
9 M N 65	Adenocarcinoma	Adenocarcinoma with radiation reaction	26 B K 53	One curettage negative Adenocarcinoma 6 mos later	Uterus 10 by 7 by 5 cm Radiation reaction with small foci of carcinoma
10 E D 71	Adenocarcinoma	Uterus 8 by 4 by 4 cm Nodule of tumor in fundus 2.5 cm Adenocarcinoma with radiation reaction of stroma Tubes and ovaries negative	27 L A 67	Adenocarcinoma	Uterus 8 by 5 by 4 cm. 3.5 cm nodule of tumor on posterior wall of uterus Adenocarcinoma of fundus radiation reaction of cervix
11 S A 58	Adenocarcinoma	Uterus 9 by 5 by 4.5 cm Adenocarcinoma with radiation reaction Tubes and ovaries negative	28 G S 44	Adenocarcinoma with foci of carcinoma simplex	Uterus 8 cm long Adenocarcinoma with radiation reaction Negative tubes and ovaries
12 E B 49	Carcinoma simplex	Uterus 9 by 6 by 3.5 cm Fundus filled with polypoid tumor Adenocarcinoma with foci of carcinoma simplex. Negative tubes and ovaries	29 M H 59	Adenocarcinoma	Uterus 9 by 5 by 3.5 cm Adenocarcinoma in one cornu with radiation reaction of uterine wall
13 E L 58	Adenocarcinoma	Uterus not measured Adenocarcinoma with deep invasion of myometrium	30 J H 65	Adenocarcinoma	Uterus 7 by 3.5 by 3 cm Adenocarcinoma with radiation reaction
14 S M 65	Adenocarcinoma	Uterus 7 by 5 by 3.5 cm Adenocarcinoma and radiation reaction Negative tubes and ovaries	31 M S 65	Adenocarcinoma	Uterus 8.5 by 4.5 by 3 cm Tumor in left cornu Adenocarcinoma showing radiation reaction Negative tubes and ovaries Biopsy from vagina showed recurrence 18 mos later
15 E H 53	Adenocarcinoma	Uterus 10 by 5 by 4 cm Adenocarcinoma with radiation reaction	32 L A 73	Adenocarcinoma	Adenocarcinoma of endometrium radiation reaction of cervix
16 A M 64	Adenocarcinoma	Uterus 9 by 7 by 4 cm Adenocarcinoma with radiation reaction Tubes and ovaries negative	33 M R 51	Adenocarcinoma	Adenocarcinoma with radiation reaction Negative tubes and ovaries
17 R W 74	Adenocarcinoma	Uterus 7 by 4.5 by 3 cm Bulky tumor mass in fundus Adenocarcinoma with radiation reaction Tubes and ovaries negative			

therapy The task of holding several applicators in place, especially when one cannot be sure what part of the uterus is involved by the tumor or how extensive it is, is rather formidable This point was discussed at length by Sampson in 1934, who said, "Variations in the situation of the carcinoma

and the degree of its invasion, which can be realized only by the laboratory study of the ovaries, tubes, and uterus, often make the intimate application of the radium to all of the growth a matter of chance or even impossible." He conducted many tests on excised uteri, by filling the cavity

with sodium iodide solution, then placing radium capsules therein with every effort to distribute the capsules over the endometrial surface. Roentgenographs were then made so that the size and shape of the cavity as well as the distribution of the capsules, were revealed. He concluded that

at best, the adequate filling of the uterine cavity with the capsules is a matter of chance, even in uterine cavities not distorted by submucous myomas, polyps, and carcinoma. Benign uterine tumors are of course very common in the age group in which cancer of the endometrium occurs.

In 184 patients operated on for cancer of the corpus, Sampson found 13 cases of secondary cancer of the tubes and ovaries, in which locations the tumor could hardly be expected to receive an effective dosage from intrauterine radium. There were implants in the tubes and ovaries in 2 of our cases. This point has been mentioned by others as a further reason why hysterectomy should be done on all operable patients after irradiation. While in many cases the radium can, with proper technique, be placed in close proximity to the entire tumor there can be no certainty of it in an individual case.

From the material which has come to this laboratory one must conclude that even though the radium was placed close to the tumor as it must have been in a fair proportion of cases, an adequate dose was not delivered. It has been stated that 3500 to 4000 milligram hours should be the upper limit of dosage because of the danger of fistula formation, peritonitis, or other complication which will prevent subsequent hysterectomy or add to the dangers of it.

Heyman has used multiple applicators for the radium since 1934 and has found an increase in the survival rate since he changed from the single applicator technique (8). Thus, we may expect further improvement in the technique of preoperative radiation therapy for uterine body cancer and at present there is no agreement on the most satisfactory method. At present we have some advocating only intracavitary radium, others a combination of radium plus roentgen therapy and at least one author believing that roentgen rays alone should be used before operation (1). Still others believe that roentgen rays should be used after the removal of the radium-treated uterus.

In 1937 Heyman (7) reported on 65 patients treated at the Radiumhemmet by operation and postoperative irradiation. The latter consisted in most cases of one vaginal application of radium plus roentgen rays to 3 or 4 pelvic portals. The results were 78.5 per cent 5 year cure 6

per cent 10 year cure. Moreover this group included 10 patients who had a subtotal rather than a complete hysterectomy the chief reason for this being an error in preoperative diagnosis. He said, "On account of the results thus demonstrated, we feel justified in advocating that cases of corpus cancer suitable for operation should be operated upon and submitted to postoperative radiological treatment."

Also of interest in this connection is the opinion of Healy (12) expressed in 1940. He feels that in grade I and II carcinomas of the fundus, surgery should be carried out on the operable cases without preliminary irradiation.

Finally, we have Heyman's latest publication (8) in which he states that he is not yet ready to advocate that the primary radiological treatment necessarily should be preferred to hysterectomy. Further on he repeats, "We do not wish to draw any conclusions as to the superiority of a primary radiotherapy to a primary hysterectomy in the clearly operable cases." This from a person with one of the widest experiences in treating cancer of the corpus with irradiation. For the inoperable and technically operable patients he recommends his present method of packing the uterus with multiple containers of radium, followed by hysterectomy when possible, in case of failure to effect a cure.

It has been claimed that intra uterine radium therapy will lower the viability of tumor cells even though the cancer is not eradicated and hence make a postoperative recurrence due to implants less likely. Our observations show the tumor to have been eradicated in 5 of 46 cases only. The irradiated tumor in some appeared less damaged than the adjacent normal tissues, in others it was viable though reduced in amount. Even in the most favorable report on the incidence of persistent carcinoma in irradiated uteri, tumor tissue was present in over half the cases at the time of hysterectomy.

SUMMARY AND CONCLUSIONS

Radiation therapy has won for itself an important place in the treatment of carcinoma of the body of the uterus. In the inoperable and technically operable groups of patients it is the only curative form of treatment available and it provides about 1 per cent and 30 to 50 per cent 5 year survivals in these respective groups.

In the operable group of patients there has been a widespread opinion for some years that preoperative irradiation, chiefly by means of intra uterine radium, followed by hysterectomy and salpingo-oophorectomy 1 to 2 months later would

accomplish a higher percentage of cures than either irradiation or surgery alone. Accordingly, this has been advocated as the method of choice for treating this type of cancer.

3. More recent publications indicate doubt as to the wisdom of using preoperative radiation therapy as a routine measure in the operable cases. Good results have been obtained from a combination of surgery with postoperative roentgen irradiation.

4. Forty-six proved cases of carcinoma of the uterine body have been reviewed, all of which were treated by intrauterine radon and complete hysterectomy at least 6 weeks after the irradiation.

5. In only 5 cases was the uterus found to be free of carcinoma when removed.

6. This investigation does not throw light on the question of the value of radiation in preventing vaginal metastases.

7. In deciding whether or not to use preoperative radiation, the relative advantages of

possibly destroying the tumor or decreasing its chance of implantation must be balanced against the delay and inconvenience to the patient.

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TREATMENT OF ACUTE APPENDICITIS AT THE UNIVERSITY OF MINNESOTA HOSPITALS

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EACH year in the United States, from 12,000 to 20,000 people die of appendicitis (28). A review of reports from a number of clinics shows that nearly 90 per cent of the total deaths occurred in patients in whom the appendix had ruptured before medical aid was sought, a group comprising about a quarter of the total admissions. Among the patients in this collected series without clinically evident extension of the process beyond the appendix itself the mortality ranged from 0 to 0.8 per cent in the various clinics, while in those patients with extra-appendical extension, either with localization as in abscess formation or with spreading or generalized peritonitis, it ranged from 10 to 27.3 per cent, with an average of 14.3 per cent (2, 4, 8, 10, 12, 14). The overall mortality rate varied from 2.5 to 6.3 per cent with a mean of 4.15 per cent. In view of the increased mortality rate among cases with extra-appendical extension, we are reviewing the records of the University of Minnesota Hospitals particularly with regard to this group. In this group the statistics in cases of therapy by operative as contrasted to conservative measures may be compared in our own hospital.

ETIOLOGY

Many theories have been advanced to explain the occurrence of appendicitis. They vary from embolic infection to abnormal fat metabolism (obstruction of the lumen, but the only means by which appendicitis comparable to that seen clinically has been produced experimentally is through luminal obstruction. It has been shown at this clinic (6, 20, 21) that the disease may be produced regularly in man, the rabbit, and the chimpanzee by ligation obstruction of the lumen, spurring the blood supply. In these 3 species, the appendiceal mucosa is capable of secreting fluid against elevated pressures. In a large group of other species, among them the gibbon, none was found in which the appendix or cecal pouch had this property and in them appendicitis regularly did not follow upon obstruction (7). Dennis, Baileg Varco and Wangenstein have shown that in the

rabbit increased intraluminal pressure occludes some of the vessels in the appendiceal wall, leading to areas of ischemic necrosis, which offer an open field to whatever bacteria happen to be present, and which also offer weakened areas through which perforation may occur. Similar changes occur in man.

The nature of the obstructing mechanism in clinical appendicitis was found by Wangenstein and Bowers (19) to be cicatricial stenosis with or without fecaliths in 100 per cent of gangrenous specimens. In a group presenting acute inflammation without gangrene, longitudinal section after formalin fixation failed to show luminal obstruction in 28 per cent of the specimens. Dennis has presented evidence that many of this last group present a spastic muscular obstruction of sufficient degree to account for the appendicitis observed. Other mechanisms are occasionally found, such as kinks from adhesive bands. Edema of the lymphoid tissue of the appendix, paralleling general lymphoid enlargement, has been stressed by Gray and Helfetz. Finally a certain number of cases of appendicitis may rest on some basis other than obstruction.

FACTORS IN EXTRA-APPENDICAL EXTENSION

A number of uncontrollable factors are involved in the occurrence of extra-appendical extension in appendicitis. Few if any, cases of appendicitis resulting from spastic or other low-grade obstruction proceed to perforation or gangrene (5). On the other hand, nearly all cases in which complete luminal obstruction has occurred, whether from stricture or from stricture plus fecalith, and in which the secretory capacity of the appendiceal mucosa is normal, proceed to perforation or gangrene when appendectomy is not performed.

The identity of the predominant organism in the appendiceal lumen at the time of onset of appendicitis is another uncontrollable factor, probably not of importance in the promotion of perforation, but certainly of great consequence with regard to the influence of the resultant peritonitis.

Two controllable factors are also of importance in extra-appendical extension: time and purg-

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tion If appendectomy is performed early enough in the course of the disease, sufficient time for extension is not allowed Purgation after the onset of appendicitis is commonly considered to increase the mortality steeply Bower found that of those patients with acute appendicitis who took no cathartic, 1 in 80 died, of those who took one cathartic, 1 in 15 died, and of those who took more than one cathartic, 1 in 7 died In so far as we have been able to find, no evidence has been presented to show that rupture occurs earlier if cathartics are used Some experiments on rabbits suggest, however, that the increased mortality observed in man following the administration of cathartics in the presence of appendicitis may be explicable on the basis of increased bowel activity and consequent prevention of walling off of the process after perforation (6)

In many instances in which appendectomy is not performed, the inflammatory process subsides spontaneously Evidence has been found in the case of the rabbit that diminution or cessation of fluid secretion occurs under the influence of prolonged intraluminal pressure elevation insufficient to cause rupture (6) Similar though less conclusive evidence of such a diminution in secretion rate has been found in man Seepage of fluid through the appendical wall has also been shown to occur at the pressures involved (5) Such occurrences, as well as localization of the process by adhesions after perforation, go far to explain the success which follows the conservative treatment of late cases

DIAGNOSIS OF APPENDICITIS WITH EXTRA-APPENDICAL EXTENSION

The present policy at the University of Minnesota Hospitals is to perform appendectomy in all cases in which extension of the process has not occurred and in cases in which it is uncertain whether extension has taken place On the other hand, those cases which present evidence of spread beyond the appendix are treated by conservative means This policy requires some discussion of standards of diagnosis

Inasmuch as appendicitis is primarily a closed loop obstruction without interference with the main fecal stream, the initial findings are tenderness and more or less cramp-like pain, with localization of the pain in the right lower quadrant only after the elapse of some hours Only after the ischemic necrosis secondary to increased intraluminal pressure has set the infective factors in motion may one expect to find fever, increase in pulse rate, and elevation in the leucocyte count

The majority of patients with generalized peritonitis of appendical origin exhibit generalized abdominal pain and tenderness, absence of peristaltic sounds on auscultation of the abdomen, rebound tenderness without reference on both sides of the abdomen, tenderness on both sides on rectal examination, and distention

Localization of the process is indicated by limitation of rebound tenderness to the appendical region or reference of the pain to this region after sudden release of pressure from other areas of the abdomen Mass formation, palpable on either abdominal or rectal examination, is strong evidence of localization, but its presence is dependent on the duration of the illness

We have gained the impression that the condition within the abdomen may be accurately described in the majority of cases on the basis of history and physical and laboratory examinations Patients seen in the first 48 hours who present limitation of appreciable spasm, tenderness, and rebound tenderness to the right lower quadrant are considered free of extension of the disease, and are treated operatively Similar treatment is accorded such patients who in addition appreciate pain in the right lower quadrant upon sudden release of pressure from other areas of the abdomen The appreciation of pain at the site of sudden release of pressure from all areas in the abdomen is evidence of generalized spread and dictates conservative management Generalized spasm and tenderness appear after generalized nonreferred rebound tenderness and indicate a well developed peritonitis

If no other cause for fever and leucocytosis is present, and if, as is usually the case, the obstruction to the appendical lumen lies proximally and the bulk of the organ is therefore involved, the level of the leucocyte count is usually a reliable index of the presence or absence of gangrene, counts of 20,000 or more per cubic millimeter indicating gangrene Leucocyte counts much above this level often imply perforation in addition In the few instances in which only the distal portion of the appendix is involved, this is not a reliable index, the process usually being more advanced than the count would indicate

Elevation of the pulse above 120 per minute and fever above 102 degrees F, taken by mouth, are corroborative points strongly suggestive of extension

Signs, symptoms, and laboratory findings have been found to be very unreliable at the extremes of life, and we are more prone, therefore, to use operative therapy in these groups than in the middle age groups

TABLE I—MORTALITY OF ACUTE APPENDICITIS AT THE UNIVERSITY OF MINNESOTA HOSPITALS

Clinical diagnosis	Cases		Deaths	
	Number	%	Number	%
A. Perforated appendicitis ("interval")	11	46		
B. Acute appendicitis without extension	11	57	6	26
C. Appendicitis with extension	(107)	(11.10)	(1)	(0.45)
I With localization	39	10.6		23
II With general peritonitis	68	3		20
Total	129	100	27	16

TREATMENT OF APPENDICITIS WITH EXTRA APPENDICEAL EXTENSION

The loss of a few slightly ill patients with extra appendiceal localized processes in 1931 and 1932 led to the introduction of conservative management for such cases at the University of Minnesota Hospitals. The wisdom of such a change is supported by the figures of Stanton, which show a rising mortality rate following appendectomy as the interval between onset of the disease and operation increases, a maximum being reached at 4 and 5 days. As Adams and Bancroft have indicated, conservative therapy at this hospital differs somewhat from that advocated by Ochser. Conservative treatment in the cases reported in the present paper includes the following items: (1) rest in bed, in the supine position (2) hot packs applied continuously to the abdomen (3) constant gastric or duodenal suction applied to an intubating duodenal tube (4) clear liquids by mouth in limited quantities—10 liters daily (5) parenteral glucose and sodium chloride solution sufficient to maintain an adequate urinary output (6) morphine or codeine as needed for pain (7) repeated small transfusions, as often as every day or two in the sicker patients (8) drainage of abscesses only if they cause appreciable fever or increase in pulse rate (9) sulfanilamide (used in only 6 of the 107 cases in this series) (10) oxygen occasionally and (11) maintenance of an adequate parenteral intake of protein nitrogen (as plasma) calories (as 20 per cent glucose solution intra-venously) and vitamins [This has been attempted in only the most recent cases, a small proportion of those reported].

When the temperature has returned nearly to normal and clamping of the nasal tube can be tolerated for several hours at a time suction is discontinued, and the oral intake is cautiously increased in the succeeding 3 or 4 days as far as a

soft diet, usually with an ounce of mineral oil twice daily. If this is tolerated, patients are dismissed with this diet and directions to avoid undue exercise. They are given appointments to return to the hospital in 6 weeks for appendectomy. Of the present group, only 13 per cent failed to keep the return appointment; one of these returned a year later with generalized peritonitis, which he again survived.

RESULTS

From January 1, 1935, to July 1, 1938, 1313 patients were admitted to the University of Minnesota Hospitals. They are classified into the following clinical diagnosis groups:

- A. Perforated appendicitis ("interval cases")
- B. Acute uncomplicated appendicitis, or
- C. Appendicitis with extra appendiceal extension, either
 - Group I. Those presenting appendicitis with extra-appendiceal localization (abscess or local lord peritonitis) or
 - Group II. Those presenting appendicitis with generalized peritonitis.

Of a total of 353 interval cases, the specimens from 30 were considered normal on pathological examination, and in the remaining 223 they were termed suppurative or healing (Table I).

There were 753 cases of clinically acute appendicitis without extension. In 72 the specimens were termed normal on gross and microscopic examination (these may have been errors in diagnosis, or possibly the condition was too early to present polymorphonuclear leucocytic infiltration of the appendiceal wall) (20). In 92 instances, healing processes or subsiding inflammation were found. In 463, acute suppurative appendicitis proved to be present, and in 124, frank gangrene had developed. In these 753 cases, 6 deaths occurred. The postmortem examinations established the following causes of death: paralytic ileus, acute right heart failure, cyclopyrrolone death, bronchopneumonia and heart failure, b) perityphilitis considered due to hypothalamic cysts, and portal vein thrombosis and uremia. All 6 deaths occurred in adults, the mean age being 35 years.

In the remaining 207 cases, a diagnosis of appendicitis with extra-appendiceal extension was made in 178 on the basis of history and physical

¹As the statistics presented the term "interval cases" refers to patients treated conservatively elsewhere or in our hospital during some previous time. Patients with appendicitis with extension, who have returned later to be treated conservatively in our hospital, and whose specimens in the present appendectomy series, show original characteristics in the postoperative specimens in this paper. No such patients have been lost at appendectomy.

²As will be apparent from the work of Dr. J. E. Tamm, associate professor of histopathology at the University of Minnesota, his studies have shown that the histological appearance and chiefly the pronounced

TABLE II—TREATMENT AND OUTCOME OF PATIENTS PRESENTING APPENDICITIS WITH EXTRA-APPENDICULAR EXTENSION*

Treatment	Group I Extra-appendicular localization				Group II Generalized peritonitis			
	Cases		Deaths		Cases		Deaths	
	Num- ber	%	Num- ber	%	Num- ber	%	Num- ber	%
Immediate appendec- tomy with drainage at time	10	7.2	0	0	4	4.9	2	50.0
Immediate appendec- tomy without drainage	13	9.4	2	15.4	2	2.9	0	0
Conservative without drainage	100	71.9	1	1.0	52	76.5	10	19.2
Conservative with drainage of abdom- inal abscesses	14	10.1	1	7.1	7	10.3	1	14.3
Conservative with proctotomy	1	0.7	0	0	3	4.4	0	0
Conservative with colpotomy	1	0.7	0	0	0	0	0	0
Totals	139	100.0	4	2.88	68	100.0	13	19.1

*Of the 10 patients with extra appendicular localization treated by appendectomy with immediate drainage, 2 subsequently developed abdominal masses necessitating drainage by the abdominal route. Two conservatively treated cases were given paroral sulfanilamide solution. Of the 2 patients with generalized peritonitis that died following appendectomy with immediate drainage, both developed inflammatory masses after appendectomy, 1 of which was drained through the abdomen the other by colpotomy. Four conservatively treated patients with generalized peritonitis were given sulfanilamide, 1 died.

and laboratory findings, and in 29 instances upon laparotomy performed because doubt was present whether extension had occurred. There were 17 deaths in this group. Inasmuch as this is the group in which most of the deaths occurred, special emphasis will be placed upon it.

DETAILS OF MANAGEMENT OF CASES OF APPENDICITIS WITH EXTENSION

The details of management of the group presenting appendicitis with extension are given in Table II. Twenty-three patients, with extra-appendicular localization were subjected to immediate appendectomy, in 13 of these the wounds were closed without drainage and of these, 2 died. In the remainder drainage was applied and the patients survived. Six patients with generalized peritonitis also were subjected to immediate appendectomy, and all survived except 2 of the 4 cases in which the wounds were closed with drainage.

Most of the conservatively treated patients, whether with or without localization, recovered without drainage. Of those that were treated

TABLE III—ANALYSIS OF DEATHS IN APPENDICITIS WITH EXTENSION

	Group I Extra appendicular localization	Group II Generalized peritonitis ¹
Number of deaths	4	13
Number of adults	4	6
Number of children	0	7
Number of males	2	8
Number of females	2	5
Average age of adults— years	40	37.6
Average age of children— years	—	10.0
Autopsies—per cent	100	100

¹Two deaths in group I were ascribed to peritonitis, 1 to pneumonia and 1 to gas bacillus infection of the abdominal wall. Contributing factors were eversion perforation of the bowel, mechanical bowel obstruction, hydrothorax and aortic aneurysm.

Ten of the 13 deaths in group II were ascribed to single dominant factors. These were peritonitis in 7 cases, paralytic ileus in 2 cases, and septicemia in 1. Contributing factors were perforation of the bowel, eversion, empyema, lung abscess, liver abscess, thrombophlebitis and hydrothorax.

with drainage, whether by laparotomy, colpotomy, or proctotomy, the numbers are too small to be of statistical significance (Table II).

Sperling and Myrick reported that the mean hospital stay in uncomplicated cases was 9.75 days, while in patients with extension the mean stay was 22.5 days, including the return appointment for appendectomy. In our series of cases of appendicitis with extension, the mean time was 17.7 days for patients with localization and 23.1 days for patients with generalized peritonitis. These figures do not include the return appointment for appendectomy. Conservative management is therefore a more time-consuming course to follow than immediate appendectomy.

COMPARISON OF CONSERVATIVE WITH OPERATIVE THERAPEUTIC RESULTS IN THE TREATMENT OF APPENDICITIS WITH EXTENSION

Of 29 patients with extra-appendicular extension treated by immediate appendectomy, 4 died, a mortality rate of 13.8 per cent. Of 178 cases in which the examiner felt sure that extension was already present upon admission, and in which conservative therapy was therefore used, 13 died, a mortality of 7.3 per cent. The mortality rate, moreover, was lower with conservative therapy in each group than with immediate appendectomy.

ANALYSIS OF DEATHS IN APPENDICITIS WITH EXTENSION

Of 69 children presenting appendicitis with extra-appendicular localization, none was lost, but in 70 adults in this category, the mortality was 5.7 per cent. The mortality rates in generalized peritonitis were 17.5 per cent among 40 children,

TABLE II.—SUCCESSIVE STUDIES ON MORTALITY FIGURES IN ACUTE APPENDICITIS AT UNIVERSITY OF MINNESOTA HOSPITALS

Types of appendicitis	1929-1939 (47)		1931-1935 (11)		1937-1939	
	Cases	Mortality %	Cases	Mortality %	Cases	Mortality %
Acute uncomplicated and interstitial cases	47	4.8	24.1	2.9	166	5.4
Cases with extra-appendiceal extension						
5-month Incision Late	166	3.6	109	2.7	20	
11-month general peritonitis		2.1	64	3.3	66	2.9
Total	208	3.4	138	3.6	182	3.1

and 21.4 per cent among 38 adults. There were 86 males and 53 females with localization and 45 males and 23 females with generalized peritonitis. There was no significant difference between the sexes in mortality. All deaths in all groups of patients were followed by autopsy. An analysis of the deaths in our series of cases is presented in Table III.

CONSERVATIVE MANAGEMENT OF ADVANCED APPENDICITIS PREFERRED

The figures presented in the present paper are distinctly better than those reported from this clinic either by Taache and Spanio for the years 1920 to 1929, when all patients were appendicetomized, or by Sperling and Myrick for the years 1931 to 1935, the period just after the introduction of conservative therapy for advanced cases (Table IV). Although a part of this improvement is due to inclusion of a larger number of less advanced cases in the present series, nevertheless the mortality rates in the cases with extra-appendiceal extension, whether localized or generalized, have fallen materially. Several factors are of importance. Blood transfusion has been more freely used in the first place, and greater care has been given to a proper salt intake and to a less extent to a proper caloric intake by the paroral route. It is felt that a large part of this improvement, however, is due to a more adequate understanding of the pathogenesis of the disease.

As stressed by Sperling and Myrick, abscesses are drained only by extraperitoneal routes and only when in addition to local evidences, fever and elevation of pulse and leucocyte count are present. The McBurney incision exclusively is used for appendectomy, for it gives adequate exposure and can easily be enlarged if need be.

The policy here is to omit drainage unless there is definite indication for it.

Although considerable improvement over previous results is reported in this paper, the experience of Thompson, Brabson, and Walker with the combined use of sulfanilamide and drainage at immediate appendectomy suggests that still more satisfactory methods of treatment of patients with appendicitis with perforation may be at hand.

In our group of children with localized processes we have had no deaths in the present series. We have gained the impression that conservative management is more efficacious in this group than in adults with localization or patients with generalized peritonitis, but our mortality data are not large enough to be statistically significant in this respect. Miller and his associates concluded that conservative therapy is more satisfactory for localized than for generalized peritoneal infection, and the data of Adams and Bancroft also support this conclusion.

Comparison of the results of conservative therapy with those of more radical methods both here and at most other clinics suggests that this is the method of choice in cases in which the process has spread beyond the appendix itself. This is borne out by the fact that there were 29 cases in the present group in which sufficient doubt concerning the exact status of the disease existed so that operation was performed and appendectomy done in the presence of abscess or peritonitis in this group the mortality was 13.8 per cent. The mortality rate in the 178 conservatively treated cases with frank extension, and therefore usually with more advanced disease on the other hand, was 7.3 per cent. It is such data that cause us to favor the conservative management of advanced cases of appendicitis in spite of the extra cost in terms of patience, drugs, blood, and days in the hospital.

CONCLUSIONS

1. A review of 133 cases of clinical appendicitis in which patients are treated at the University of Minnesota Hospitals from January 1, 1935, to July 1, 1939, shows an overall mortality rate of 1.75 per cent.

Conservative management of the most advanced cases has been the rule. The mortality rate in cases with extra-appendiceal localization (localized peritonitis or abscess formation) was 3.6 per cent, and that in cases with generalized peritonitis was 9.1 per cent.

2. In spite of the fact that it requires the expenditure of more hospital days, drugs, blood, and

care, conservative therapy is probably the treatment of choice in cases of appendicitis with spread of the disease beyond the appendix itself

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THE CIRCULATION IN NORMAL AND VARICOSE VEINS

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A RECENT review of the literature on the physiology of varicose veins of the leg describes certain phases of the problem which need further clarification (5). Herein is reported the first of a series of studies which have been undertaken to establish a clearer picture of fundamentals and a sounder foundation on which to base treatment.

ANATOMY

The anatomical relationships in the leg are well adapted to perform the necessary functions of that structure, yet because of the close integration of the units involved in the venous circulation, relatively mild interference with these elements will often disrupt the activity of the whole mechanism. It is not proposed to cover completely the anatomy of the veins of the leg, but to indicate the intimate co-ordination existing between veins of the foot and leg with the muscles and fascia.

The superficial veins arise from the dorsal superficial arcade of the foot. This arch lies upon the extensor tendons of the toes which in turn cover a deep group of veins consisting mainly of the *dorsalis pedis* (from which arises the anterior tibial) and numerous perforating vessels. On the plantar surface there is an arcade located at the level of the metatarsophalangeal joints and consists of a large lateral and a smaller median vessel. Communicating veins connect the plantar arch with the dorsal plexus to form a complete circle around the metatarsal bones. In addition, the lateral plantar vein anastomoses with the *dorsalis pedis* through a large vessel which perforates the foot at the base of the first interspace (between the first and second metatarsals).

Around the ankle is a complex and variable series of anastomoses of the long and short superficial veins with both the anterior and posterior tibial vessels (Fig. 1). These communications are adapted to serve as auxiliary or by-pass channels should some local obstruction arise as after a fracture or thrombosis.

In the leg there are three main deep venous trunks. The anterior tibial vein arises from the *dorsalis pedis* and passes upward under the ten-

dons of the long extensors of the toes and onto the lateral surface of the tibia and the anterior surface of the interosseous septum. It passes through the septum near the head of the tibia and empties into the lowest segment of the popliteal vein. The posterior tibial, formed mainly from the plantar tributaries, passes upward along the posterior surface of the septum and enters the popliteal at or near the junction of the anterior tibial. A third channel, the peroneal arises just above the ankle posteriorly and ascends parallel to the peroneus muscles to empty into the popliteal vein at the same level as the two other trunks.

In addition to these *intermuscular* veins, there are important *intramuscular* channels which are of two types. In all the muscles of the leg except the *gastrocnemius* and *soleus* there are numerous fine veins which leave the muscle at right angles to the fibers. The branches of these vessels form a network within the muscle so that a series of arcades connect with the main trunks. These are the vessels which may enlarge and form new channels if an obstruction should occur.

Dissection of the veins within the *gastrocnemius* and *soleus* shows an arborized plexus of large thin walled vessels which traverse nearly the length of the muscle belly and exit close to the upper pole (Fig. 2). These veins are most effectively emptied by muscular activity and contribute a great deal to the maintenance of the normal velocity of flow.

It is well established that muscular activity is a major force in the propulsion of venous blood. The *gastrocnemius* and *soleus* have attachments which make them particularly effective for this purpose. They have a very large range of motion and consequently an unusual ability to exert effective compression.

Around the leg is a strong layer of fascia (*fascia cruris*) which forms a semirigid, rather inclusive envelope. This layer is continuous with the *fascia lata* and with the deep fascia of the foot. It is attached firmly along the anterior margin of the tibia, to the bony prominences of the knee, and to the malleoli to form a chamber which almost completely encloses the deep structures of the leg. This layer tends to limit the effect of contracting muscles to the elements enclosed. Veins outside the fascia are lightly supported and tend to move away when the thickened muscle belly begins to

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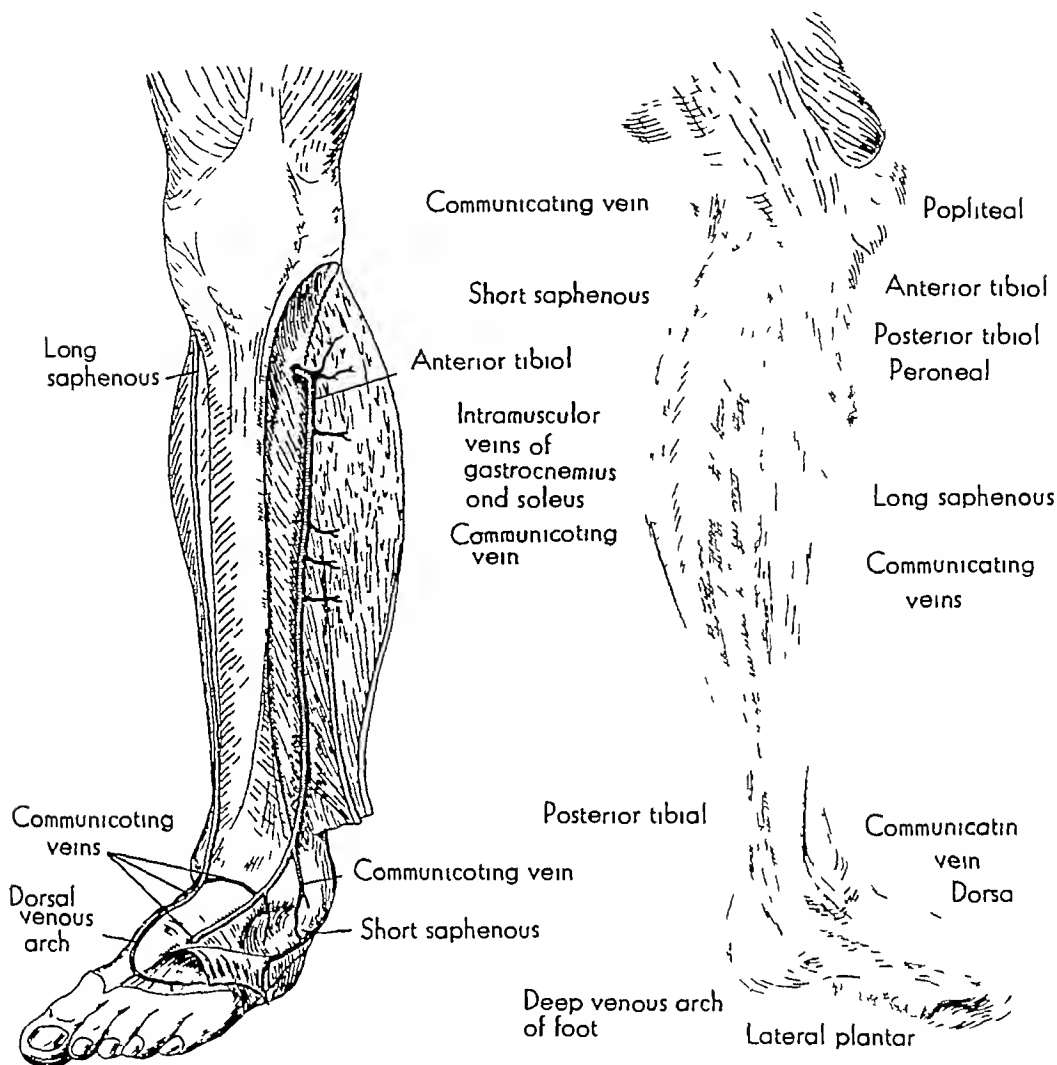


Fig 1 A dissection of the foot and leg to show the relationships of the deep and superficial venous channels

Note particularly the arrangement of tributary communications

compress the vessel. Therefore, the superficial veins are less completely emptied by this force than are the deep.

In the thigh there is a similar though less perfect system. Large veins are present within the muscles and between muscle planes (especially of the quadriceps group) so that activity probably effectively empties them.

THE VELOCITY OF CIRCULATION

It is universally accepted that gravity is most important in impeding the venous return. In the

erect position, blood must be elevated against a pressure of 5 centimeters of water. This is accomplished by the action of muscle groups segmented along the major trunk veins. Muscles supply a propelling impulse which is effective by valvular control of the flow.

Circulation time studies emphasize the effect of gravity on the venous circulation. Sweeney, and Toth, using the tilting table, found that the circulation time (foot to heart)

TABLE 1—LEG TO THROAT CIRCULATION TIME (WITH NEO CALGLUCON) 40 INDIVIDUALS WITH VARICOSE VEINS, STANDING POSITION

TABLE I—RESULTS OF TENDLENBURG TEST WITH VARICOSE VEINS, CONTINUED				
Case	Trendelenburg test	Size of vein	Time from beginning of injection to appearance of sensation	Effect of muscular activity
			22 sec.	Licking intensif. of sensation
	Negative	++	none	Kicking intensified sensation
	Negative	++	none 47 sec.	Kicking did not affect sensation
	Negative	++	1 min.	Licking intensified sensation
	Negative	++	1 min.	Walking did not increase sensation
	Negative	+		
	Positive	++	27 sec.	Walking increased sensation
	Positive	++	none	
	Positive	+	none 33 sec.	Licking intensified sensation
	Positive	++	none 44 sec.	Standing on toes increased sensation
	Positive	+	none	Licking intensified sensation
	Positive	+	none 48 sec.	Walking increased sensation
	Positive	++	1 min.	Standing on toes increased sensation
	Positive	+	1 min.	
14	Positive	++	none	Walking did not increase sensation
	Positive	+	none	Standing on toes increased sensation
15	Positive	++	none	Standing on toes increased sensation
17	Doubly positive	++	none	Standing on toes increased sensation
18	Doubly positive	++	none	Walking intensified sensation
19	Doubly positive	++	none	Walking did not increase sensation
20	Doubly positive	++	2 min.	
Stand with toes on a raised surface when walking around for 10 min.				

Hand over toes

	Positive	++	No sensation within 1 min. after injection	Scall on reaction after walking around for 10 min.
	Positive	+	No sensation within 10 min. after injection	Walking did not bring on reaction
	Positive	++	No sensation within 10 min. after injection	No reaction after 10 min's walk
	Positive	++	No sensation within 10 min. after injection	No reaction after 10 min's walk
24	Positive	++	No sensation within 17 min. after injection	No reaction after 10 min's walk
	Positive	++	No sensation within 10 min. after injection	Walking did not bring on the reaction
26	Doubly positive	+	No sensation within 10 min. after injection	

The effect of muscular activity on the timing of the superficial veins

27	Negative	++	No sensation within 10 min. after injection	Appeared immediately after licking 1 time
28	Positive	+	No sensation within 10 min. after injection	Appeared immediately after licking 10 min.
29	Positive	++	No sensation within 10 min. after injection	Appeared immediately after licking 5 times
30	Positive	++	No sensation within 10 min. after injection	Appeared 10 sec. after licking 10 min.
31	Negative	++	No sensation within 10 min. after injection	Appeared 10 sec. after lick no 1 time
	Negative	++	No sensation within 10 min. after injection	Appeared 10 sec. after standing on toes 10 min.
32	Positive	++	No sensation within 10 min. after injection	Appeared 10 sec. after standing on toes 10 min.
33	Positive	+	No sensation within 10 min. after injection	Appeared 10 sec. after standing on toes 10 min.
34	Positive	++	No sensation within 10 min. after injection	Appeared 10 min. after standing on toes 10 min.
35	Negative	++	No sensation within 10 min. after injection	Appeared immediately after licking 10 min.
36	Negative	++	No sensation within 10 min. after injection	Appeared immediately after licking 10 min.
37	Positive	++	No sensation within 10 min. after injection	Appeared after standing on toes 10 min.
38	Positive	+	No sensation within 10 min. after injection	Appeared 10 sec. after licking on toes
39	Doubly positive	++	No sensation within 10 min. after injection	

in variability of this test is so great that only general conclusions may be drawn from the results.

vertical position was as much as 6 times slower than in the horizontal. Readings in the horizontal varied between 20 and 40 seconds. In the vertical, in 11 cases, the circulation was so retarded that no sensation was elicited after 221 seconds. However, when these cases were returned to the horizontal, a strong reaction appeared within 10 to 41 seconds.

Bock, Dill, and Edwards likewise found marked slowing in the erect position. In some cases, a standing circulation time of 5 to 7 minutes was noted. In others, no reaction was noted when the subject was standing, yet when he assumed the horizontal, it appeared within 25 seconds. Thus, in the normal long saphenous vein, gravity markedly retards the flow when there is little or no muscular activity.

A study of the rate of circulation in varicose veins has yielded further information on the effect of gravity and the pumping action of the muscles. Five cubic centimeters of 20 per cent calcium gluconogalactogluconate, so called neocalglucon, was rapidly injected into varicosities in the calf of the leg. The circulation time was taken from the beginning of the injection to the moment when the sensations of warmth and sweet taste were noted by the individual. All patients were tested in standing position. Results are shown in Table I.

These records indicate that the velocity of flow in varicose veins is variable, though generally slower than in the normal (2, 9). There is apparently little correlation between the size of the vein and velocity. In 6 of 26 cases, blanks occurred, that is, the subject noted no sensation after standing quietly or even walking around. This is evidently due to dilution of the solution as it is slowly carried upward. A concentration is reached which is below the threshold of the reaction.

In most cases the effect of muscular activity on the emptying of the superficial veins is nicely demonstrated. Kicking, standing on the toes, or walking, intensified the reaction once it had appeared. In other individuals, if no sensation was noted within 2 minutes, the reaction could be brought on almost at once by some muscular activity.

This study clearly indicates the unusual degree of stasis in varicose veins in the erect position, and the rôle of muscular activity in overcoming the effects of this load.

DIRECTION OF THE CIRCULATION IN VARICOSE VEINS

The relation of the direction of flow to valvular incompetence is not established by the circulation

TABLE II—SPECIFIC GRAVITY OF SOLUTIONS PREVIOUSLY USED TO DETERMINE THE DIRECTION OF CIRCULATION IN VARICOSE VEINS

Investigator	Solution	Concentration per cent	Specific gravity
	Diodrast	35	1.185
Pomeranz and Tunick McPheeters, Merkert and Lundblad	Skiodan	40	1.258
Veal and Van Werden	Thorotrast	25	1.270
Patey, Tatham and Nicholas Herlyn	Uroselectan (Neo-Iopax)	50	1.335
McPheeters and Rice	Lipiodal	40	1.302

These determinations were made at room temperature (85 degrees F) by the pycnometer technique. Note the weight of these solutions as compared with blood which has an average specific gravity of 1.055.

time method. It has long been known that when a person with incompetent veins stood up, there was a rush of blood from above downward. This led to the vicious cycle theory (reversed circulation) which was substantiated by observations on the movement of x-ray opaque fluids injected into saphenous varicosities in the erect position. The greater mass of evidence (6, 10, 11, 12, 13, 17) favors a continuous reversal in the direction of flow in incompetent veins. However, these studies are open to criticism because of the high specific gravity of the solutions used. Schmier injected an iodized oil having nearly the same specific gravity as blood and observed a central flow in the erect position and in spite of incompetent valves. Loehr and Toelle obtained similar results with another type of opaque medium.

In order to explain the discrepancy, the specific gravity of the solutions used by past investigators was determined (Table II). All those which appeared to be carried downward were found to be considerably heavier than blood and would naturally sink through a less dense medium. These solutions would have to be diluted from 2 to 4 to 5 times to obtain the same specific gravity as blood.

It was, therefore, decided to repeat this type of experiment with a preparation having a rigidly controlled specific gravity. A sterile aqueous solution of sodium iodohippuric acid, known as hippuran, was made up with a specific gravity approximating that of the patient's blood.

Our patients were placed in the standing position for 5 minutes, after which time a sample of blood was drawn from the varicosity. The specific gravity was immediately determined by



Fig. 3. a, Film showing soft tissue detail before injection. b, At the end of an injection of 3 cubic centimeters of hippuran, with tourniquets placed above and below the puncture site, 5 minutes after removal of the tourniquets. c, 5 minutes after injection. The solution has remained practically stationary though it is slowly being diluted. Specific gravity of blood .051; of solution, .053. In all films, the site of injection is marked with lead O.

the falling drop method (without the use of anti-conglutants). In addition, the specific gravity of each ampule of test solution was determined. Roentgenograms were taken as the injection was completed and after various intervals. Test films of uninjected varicosities were also exposed to determine the degree of detail produced by the technique used. This was necessary because of the soft shadow thrown by the diluted hippuran solution.

PROTOCOLS

CASE 1. Normal saphenous vein injected with 3 cubic centimeters of solution at level of calf of leg. A film exposed at the end of the injection shows rapid filling of the vein and tributaries above the point of injection. A second film exposed 5 minutes later shows only a trace of hippuran.

CASE 2. Varicosity of the long saphenous vein with positive Trendelenburg test. Size of vein, 4+. Specific gravity of blood, .05; of solution, .053. Three cubic centimeters of solution was injected at level of the calf of the leg. A film exposed at the completion of the injection showed filling of the vein about 3/4 inches below the point of injection and 1 1/4 inches above. Ten minutes later traces were still present above the site of injection, but none as seen below.

CASE 3. Varicosity of the long saphenous vein with positive Trendelenburg test. Size of vein, 3+. Specific gravity of blood, .05; of solution, .053. Three cubic centimeters of solution was injected into the calf region after tourniquets had been placed above and below this site to localize sharply the opaque medium. A film exposed at the end of the injection showed heavy concentration in the vein around the needle. The tourniquets were removed and after 5 minutes another film was taken. This showed no change in the position of the solution. A film

exposed 5 minutes after injection demonstrated trace above the point of injection.

CASE 4. Varicosity of the long saphenous vein with positive Trendelenburg test. Size of vein, 4+. Specific gravity of blood, .05; of solution, .053. In order to reduce dilution of the medium, the tourniquets were placed 4 inches apart around the calf and cubic centimeters of blood was aspirated from the intervening segment of varicosity. This was replaced with 3 cubic centimeters of hippuran. The tourniquets were removed and 5 minutes later film was exposed. This showed heavy concentration of the solution at the level of injection. Three minutes later and after a 20 foot walk, the hippuran as found above the site of injection. Six minutes after injection, and after a total walk of 50 feet, the medium as seen in the same position but more dilute.

CASE 5. Varicosity of the long saphenous vein with positive Trendelenburg test. Size of vein, 4+. Specific gravity of blood, .05; of solution, .053. Eight cubic centimeters of hippuran was injected at calf level without the use of tourniquets. At the end of the injection, the solution appeared 3 inches above and 3/4 inches below the needle. Ten minutes later trace was still present above but none below.

CASE 6. Varicosity of the long saphenous vein with positive Trendelenburg test. Size of vein, 3+. Specific gravity of blood, .05; of solution, .053. Three cubic centimeters of solution was injected at calf level without tourniquets. At the end of the injection the solution appeared 3/4 inches above and below the needle. Ten minutes later and after 5 foot walk, trace was still noted above but none below.

CASE 7. Varicosity of the long saphenous vein with positive Trendelenburg test (both legs). Caliber of the veins of both legs, 4+. Specific gravity of blood, .053; of hippuran, .053. Two cubic centimeters of solution was injected into each leg. After injection of the right leg, the medium was found 4 inches above the needle. Five

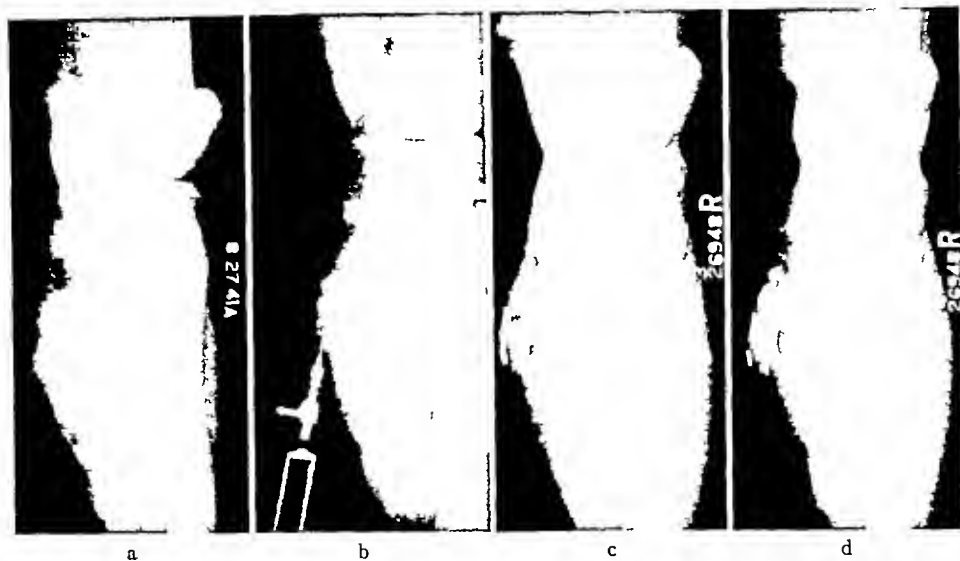


Fig 3 Case 4 a, Film showing soft tissue detail before injection. Tourniquets were then placed 4 inches apart around the calf of the leg and 10 cubic centimeters of blood was aspirated from the intervening segment of varicosity. This was replaced with 10 cubic centimeters of hippuran and then the tourniquets were removed. b, Film exposed 1 minute after removal of the tourniquets, c, 3 minutes after injection and a twenty foot walk, d, 6 minutes after injection and a total walk of 50 feet. Note that there is little shift in position of the solution but it has become more dilute. Specific gravity of blood 1.051, of solution, 1.053.

minutes later a trace was still present in the same position. One minute after injection of the left leg the solution was noted above the point of the needle. The patient was told to strain as at stool and another film was exposed which showed movement of the hippuran downward.

CASE 8 Saphenous varicosity having a positive Trendelenburg test. Caliber of vein, 3+. Specific gravity of blood, 1.053, of solution, 1.054. Four cubic centimeters was injected. After injection the solution appeared 1½ inches above and below the needle. Five minutes later a trace was still present above but none below.

CASE 9 Saphenous varicosity having a positive Trendelenburg test. Caliber of vein, 3+. Specific gravity of blood, 1.053, of solution, 1.054. Five cubic centimeters was injected just above knee. At the end of injection the solution appeared localized at the site of the needle puncture. Five minutes later a trace was still noted in the same place.

CASE 10 Saphenous varicosity with a positive Trendelenburg test. Caliber of vein, 4+. Specific gravity of blood, 1.053, of hippuran, 1.054. Four cubic centimeters was injected. After injection, the solution appeared in the vein at the level of the puncture. Five minutes later a trace of the hippuran was still present above the level of injection.

CASE 11 Saphenous varicosity with a positive Trendelenburg test. Caliber of vein, 4+. Specific gravity of blood, 1.053, of hippuran, 1.053. A film exposed after injection of 3 cubic centimeters showed all of the material above the needle. Five minutes later, a trace was still present in the same position. After elevation of the leg and then a wait of a few minutes, a second injection of 5 cubic centimeters was given at the same level. Three minutes afterward all of the solution was found above the point of introduction.

CASE 12 Saphenous varicosity with a doubly positive Trendelenburg test. Caliber of vein, 4+. Specific gravity of blood, 1.057, of hippuran, 1.057. Three cubic centimeters was injected. At the end of the injection the solution appeared above and below the site. Five minutes later a trace was still present in the same location. After kicking ten times there was still a trace present.

The accompanying roentgenograms (Figs 2 to 5)¹ substantiate the observations of Schmier, and Loehr and Toelle, and indicate the following:

- 1 In the normal saphenous vein in the erect position, there is a moderately slow centrally directed flow.

- 2 In varicose saphenous veins where the valves are still competent, the circulation is centrally directed but the velocity of flow reduced.

- 3 When the valves are incompetent, the circulation is nearly stationary. There is a very slow upward flow when the upright state has been maintained for a period of time sufficient to allow for complete filling of the vessel.

- 4 Walking does not markedly affect the direction of flow in the saphenous trunk above the calf of the leg as shown by the movement of the hippuran solution.

- 5 Coughing or straining rapidly and readily reverses the direction of flow and forces the

¹The roentgenographic studies were carried out at The Chicago Memorial Hospital where Dr. George Landau very graciously supplied necessary technical assistance and aid in interpretation of films.



Fig. 4. Case 6. a, Film exposed immediately after an injection made without the use of tourniquets. b, Fifteen minutes after injection. The fluid has moved upward but is still present in moderate concentration. Specific gravity of blood .53 of solution, .024.

opaque medium downward below the point of injection.

ANALYSIS OF STUDY

The structures of the leg are closely integrated so that the extremity forms a delicate though efficient machine. Muscles, fascia and veins have interrelated functions necessary for the maintenance of normal circulation. The pumping action of the leg muscles—especially of the gastrocnemius and soleus—is made more effective by the heavy layer of crural fascia which controls the application of muscle forces, and by valves which control the direction of flow.

Muscular activity is particularly important in overcoming the heavy load which gravity imposes on the return circulation when in the erect position. The hydrostatic head elevates the venous tension which in turn forces an increase in capillary pressure sufficient to maintain the flow of blood. The capillary pressure thus remains slightly higher than the venous tension at all times. When the patient is standing quietly the venous pressure may be elevated enough to diminish the velocity of flow to half that in the recumbent position (2, 4, 10). This change in pressure and velocity is accompanied by the collection of blood in dependent portions of the body and loss of protein-free fluid from the blood into the tissues.



Fig. 5. Case 7. a, One minute after injection of the left leg. b, Film exposed while patient is straining as at stool. The hyposmotic has been forced downward by the increased intra-abdominal pressure. Specific gravity of blood .53 of solution, .53.

Loss of fluid occurs as the pressure in the venous segment of the capillary is elevated to the point where blood pressure is higher than the colloid osmotic pressure. Lands directly measured normal capillary pressures and found an average of 43 centimeters of water pressure in the arteriolar limb and 3 centimeters in the venous side. The colloid osmotic pressure of the blood is normally 35 to 36 centimeters of water. Therefore, the pressure on the arteriolar side is 7 or 8 centimeters higher than the osmotic pressure (producing filtration) and on the venous side 9 to 10 centimeters lower (facilitating absorption). Krogh, Lands, and Turner have calculated that an excess filtration would occur at about 25 centimeters of water pressure or possibly even less because venous congestion would raise the pressure of the arterioles as well as the venules. The average normal venous pressure in the upright inactive state is well above this level as demonstrated by the experiment of Carner and Rehberg. An individual was placed standing on one foot on a low chair. The other leg hung relaxed over the edge. At intervals, venous pressures were determined on the dorsum of the relaxed foot. At the outset there was 86 centimeters of water pressure in 5 minutes, 97 centimeters and in 6 minutes, 100 centimeters. After this there was little change. During this period, fluid was lost from the blood as shown by measure-

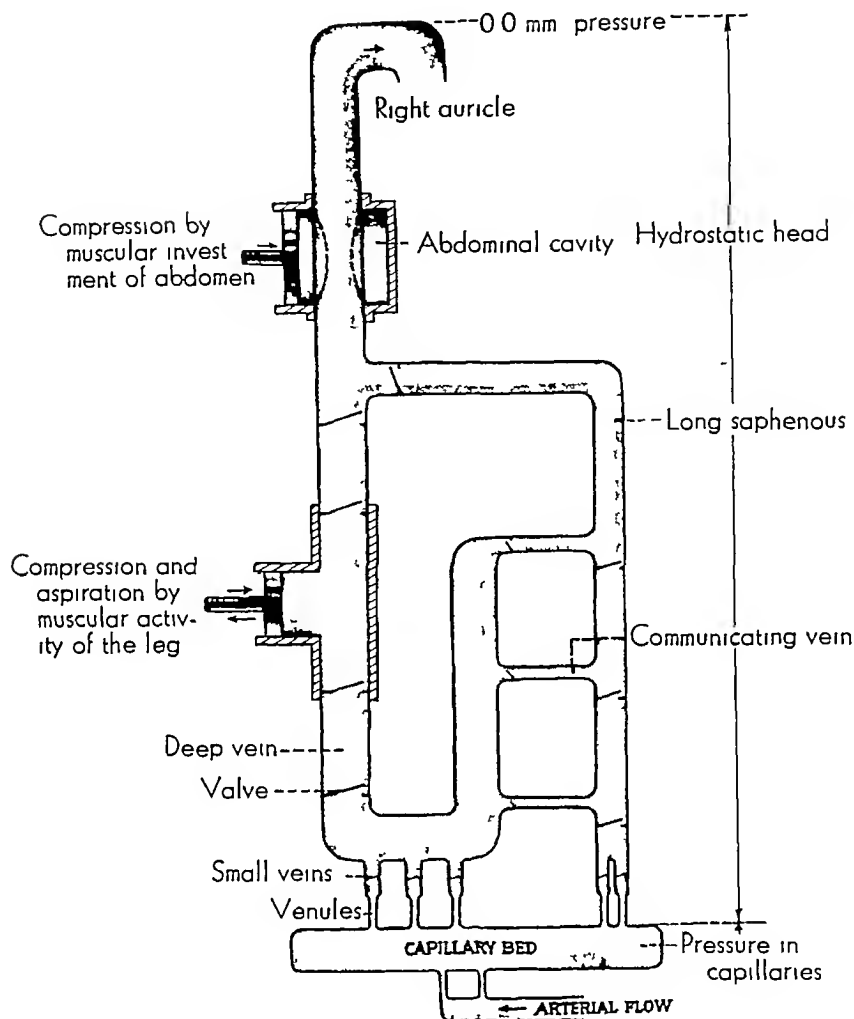


Fig. 6 Diagram of the normal venous circulation of the leg as interpreted from a mechanical point of view. Muscular activity acts as a pump which, during the compression phase, forces blood upward in the deep veins (and to a lesser extent in the superficial), and during the expansion stroke aspirates blood from the superficial veins and capillary bed. Valves prevent transmission of the compression force backward to the capillary bed and superficial veins, and support the column of blood above the active muscle elements. The saphenous trunk in the upper thigh acts mainly as an overflow pipe to carry off that blood which is not removed through the communicating veins.

Incompetence of the valves in the superficial veins permits blood to flow downward when patient moves from the recumbent to the erect position. As soon as the vessel becomes filled the flow reverses to proceed in the normal central direction. The central flow is produced and maintained by the influx of blood from the capillary bed. A rather unstable balance is thus set up which may be readily reversed. Coughing or straining, by increasing the intra abdominal pressure, may force the blood backward and down the incompetent channel. No vicious cycle exists because the superficial vessels receive more blood from the capillaries than is aspirated through the communicating veins. A continuous retrograde flow could be maintained only if blood were aspirated into the deep veins faster than filling occurs from the capillaries. Incompetence of a communicating vein impairs the pumping action of the muscles because with each compression blood is forced outward into the superficial channels rather than toward the heart. This may interfere with capillary function and produce a gross edema.

ments of the foot. At the beginning of the experiment the circumference of the foot was 27 centimeters and 15 minutes later 29 centimeters.

Thompson, Thompson, and Dailey have calculated that an average of 11 per cent of the total plasma volume may be lost in the upright inactive state in 20 to 30 minutes. Edema of the legs is not observed during walking or other muscular activity because peripheral venous pressures are reduced to a level below the critical stage.

The pumping action of muscles affects the superficial veins differently than the deep. During contraction blood is squeezed out of the deep vessels and to a lesser extent out of the superficial. During the relaxation phase, the pressure in the deep veins is reduced so that blood is aspirated into them from the capillary bed and superficial channels by way of the communicating veins. It is this aspirating action which lowers venular pressures to the level at which capillary filtration and absorption may proceed normally. This action is dependent upon proper functioning of the valves in the communicating and deep veins. Should their action be impaired, as after a thrombophlebitis, edema is apt to appear.

Because of the architectural arrangement of muscles, fascia, and veins, most of the pumping activity is confined to the lower leg. This is particularly true of the effect on the superficial trunks. The saphenous vein in the thigh is buried in soft fat, poorly supported, and provided with only a few communicating veins. Consequently, there is little compression of the vessels and limited aspiration.

All superficial veins may be considered as auxiliary to the deep channels and capable of assuming the burden of the venous return should the need arise. These vessels empty by way of either the perforating veins or through the femoral vein into the femoral or its deep tributaries. The fact that frequently the long saphenous has a smaller caliber at the fossa ovalis than lower down in the leg suggests that most of the blood in the trunk vessel is carried back through the communicating veins of the leg and that the trunk in the upper thigh acts merely as an overflow pipe. Figure 6 is a diagram in which an attempt is made to illustrate the mechanical arrangement of this system.

Varicosities of the saphenous system involve segments of either the trunk vein or its tributaries or both. The varicose portion may be considered as a simple tank or reservoir having little control over the circulation of fluid within it. This pathological arrangement is associated with pooling of large volumes of blood, slow emptying of

the vessel, eddy currents due to tortuosity and roughening of the intima, and fluctuations in pressure. When there is valvular incompetence (most cases) there is a loss in the stability of the circulation. Pressure changes which have little effect in the normal readily obstruct and reverse the direction of flow.

SUMMARY

Muscular activity is a major factor in maintaining normal capillary filtration and absorption in the erect position, and is the only mechanism which prevents the load imposed by gravity from disrupting the function of the leg.

In the recumbent position there seems to be little difference between the circulation of normal and varicose veins. However when the individual with incompetent veins stands there is an immediate rush of blood from above downward until the empty vessel is filled. Once this is complete, there is established a slow flow in the normal direction. In some patients when standing quietly it may take 20 or more minutes for the saphenous trunk to empty whereas walking or other muscular activity aspirates an appreciable volume of blood from the superficial veins and augments emptying.

This central flow is in contradiction to the vicious cycle theory. Because of the extensiveness of the capillary bed, the limitations on muscular activity and the relatively small caliber of normal communicating veins, only a portion of the blood is aspirated, and enough remains to fill the vessel and produce a slow flow upward. To maintain a continuous flow down the saphenous trunk, the communicating veins would have to draw off more blood than enters the trunk from the capillary bed. Even the increased aspiration produced by walking did not force the hippon solution downward.

Increasing the intra-abdominal pressure by coughing or straining may partially collapse the inferior vena cava and cause the transmission of a surge in pressure down the incompetent trunk (Adams) and temporarily reverse the direction of flow. It is evident that, because of the lack of support, the superficial venous tree is particularly vulnerable to variations in pressure.

Stasis pooling of blood, and the trauma of pressure surges are believed to contribute to the development of phlebosclerosis and intimal damage. These changes make the vein ready site for the onset of a typical phlebitis. This inflammation may extend and damage the blood supply of the overlying skin sufficiently to lead to a state of malnutrition which, in turn, is thought to be re-

sponsible for the cutaneous complications of varicose veins. Similarly, thrombophlebitis of the deep veins may produce the identical scarring by extension of the inflammatory reaction along the short communicating veins found around the lower third of the leg and the ankle.

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FIELD FIRE AND INVASIVE BASAL CELL CARCINOMA—BASAL-SQUAMOUS TYPE

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A TYPE of basal cell carcinoma has been observed that spreads through the derma without causing much surface ulceration and without producing much new tissue. It seems to be almost entirely destructive and to leave behind a healed area but to present an ever increasing lesion with a small raised advancing edge with intact or temporarily ulcerated epidermis. Areas may be left in the center which have broken down and remain as definite carcinomas that go on to excess tissue proliferation and invasion. Microscopic sections from the edge and any remaining areas of activity show basal cell carcinoma.

To identify this growth clinically we have called it "field fire basal cell carcinoma." It does not exactly resemble a field fire because the skin in the center and even the edge, may not ulcerate.

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Basal cell carcinoma as general occurs so frequently in the literature the other descriptions of this type could be here omitted. The closest approach to it is found in a paper by M. B. Hartwell, "Morphea-Like Epithelioma," *J. Am. Med. Ass.*, 1929, 53, 102, in which a carcinoma is reported of diagnosis of morphea turning out to be basal cell carcinoma. No photographs of lesions or photomicrographs are given.

but in the relation of a slowly advancing active edge and a center that is free of involvement, a field fire might be thought of with its burning edge and its burned out center with perhaps a few areas of remaining activity around brush piles or where any heavy growth has held the fire.

An important clinical point is that the growth may not appear very bad, its diagnosis may even be missed if no burning areas have been left in the center or a burning center may be treated without regard to the menacing advancing edge. It is thought that in reality this is an exceedingly bad growth and that it may be one of the invasive types which carries on in this fashion primarily. This viewpoint is strengthened by having observed this type of growth usually in areas in which there is not any easily invaded deep tissue, as on the scalp and nose, and in these areas themselves by having found deep invasion in which deep soft tissue had present itself such as about the orbit.

It is recognized that this is not a new type of growth but it is so interesting grossly and from points of prognosis and treatment that attention is called to it.



Fig. Field fire basal cell carcinoma: typical advancing edge; uninvolved center; deep invasion left behind (orbit). X-ray treatment, widespread surgical removal and secondary repair with thick split grafts. Patient, 67 years. Appearance could be improved with an artificial eye.



Fig. 7. left. Invasive basal cell carcinoma coming from below and destroying the repair done 9 years before following removal of the original growth.

Fig. 8. Multiple in situ basal cell growths involving the orbit. Fatal

3 years following heavy radiation given by Dr. Sherwood Moore.

The patient in Figure 3 refused operation and the growth was unaffected by radiation.

One question in consideration of this growth is that it might possibly be considered a healing carcinoma which would, of course, be a dangerous stand from the patient's point of view. Although there may be authenticated cases of healed carcinoma (perhaps many unknown ones) there is no way of knowing that any one will heal and, of course, none should be left untreated waiting for this possibility. Dunn and Smith have chosen a somewhat misleading title of this sort in reporting a single patient with a squamous growth that apparently behaved in this fashion. However

they add in the article that, "It is impossible to say what the course would have been had the lesion not been excised. One can easily conjecture that there would have been steady progress and an uncontrollable lesion."

INVASIVE BASAL CELL CARCINOMA

Invasive basal cell carcinoma is a clinical type that probably cannot be determined microscopically. It is the most important type and when once firmly established at the side of the nose about the orbit, or deep in the ear region, this growth is practically incurable at present. This point is important in prognosis and in teaching, as there has been a somewhat general idea that basal cell growths present little difficulty in treatment and in obtaining cures. By widespread surgery or radiation, these growths may be held in abeyance for long periods, but they can apparently persist in scar tissue for long periods in a dormant state and recur even after years. These late growths might be thought to be new growths entirely, but are known to occur often from deep under the surface where no epithelial cells should be. The patient in Figure 7 shows an extensive recurrence about the orbit that has come up through a flap repair of the original growth, which was done 9 years before.

The patient in Figure 8 shows a typical invasive type going into the orbit. Multiple foci often occur as seen here, sometimes the whole side of a face seems destined to form carcinomas, but the invasive tendency is the fatal factor.

It is evident that there are millions of small basal cell tumors that remain quiescent and it is probably because of these that the teaching has

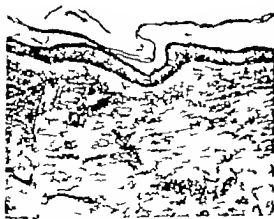


Fig. 6. Shows healed scar epithelium taken from healed center of involved area in Figure



Fig 9 Widespread multiple basal, squamous, and basal squamous growths, controlled by wide excision and split skin grafting. Patient well 6 years, but suffering more recurrences in new areas all the time.

arisen that the growths are not dangerous. However, it is possible that every basal cell lesion that takes on activity is headed toward invasive tendencies.

The old term "*rodent ulcer*" was a good one as far as clinical behavior is concerned, as the growths dig in and reappear as rodents do. This term and *Jacobean ulcer* were used for a long time before the pathology was described by Krompecher in 1903. He was the first to use the term basal cell carcinoma and to determine the origin of such growths from the basal cell layer. His general findings on skin cancers were divided into the two types now well known, and they were described as follows: (a) prickle cell cancers, which are infiltrative, metastasize to lymph nodes early, and often contain horny pearls, (b) basal cell cancers, which develop not from the transitional part of the skin and the surface, but from the deepest layers of the epithelium. Most occur on the face, cheek, forehead, and nose, and they are found usually in older people. They develop as small lumps which soon ulcerate, and for a year or 10 years thereafter grow very slowly. However, they can suddenly take on rapid growth, often mushroom like tuberosus tumors appear, and they very seldom metastasize. They develop out of small oval or spindle cells with chromatin-rich, intensively staining nuclei and have no typical prickles or intercellular bridges. Krompecher divided these basal cell growths into solid, adenoid, cystic, and parakeratotic types and a combination of these.

It is generally thought that basal cell growths originate from the basal layers of the epidermis, in fetal rests in the derma, and from hair follicles, and from sweat and sebaceous gland structures. It is possible, however, that all basal cell tumors arise from the hair follicles, as indicated by Mallory, as none seem to arise from mucous mem-



Fig 10 Section from a basal squamous carcinoma.

brane and they apparently do not occur on the palms or soles. It seems to us that the majority of them arise from the sebaceous glands, rather than from the hair forming structures in the follicles. This seems borne out by the fact that most of them occur in the so called *sebaceous area* of the face and that many of them microscopically and clinically seem to have their origin in sebaceous adenomas or plugged sebaceous glands. Rhinophyma specimens in some instances have contained multiple small basal cell lesions, and there is some experimental evidence that sterols similar to those present in sebum can, under certain conditions, be carcinogenic. The basal cell carcinomas of the buccal cavity referred to in the French literature may be adamantinomas, which in the solid type look like basal cell growths of the skin.

BASAL SQUAMOUS TYPES

Krompecher also recognized a basal squamous type. The combination of basal cell tumors with the typical squamous cancer can occur which I have observed in a tumor of the cheek" (Figs. 9 and 10).

Montgomery has studied a large series of supposed basal cell growths and has given the following conclusions: (1) Basal cell epithelioma may through metamorphosis become a basal squamous epithelioma or even a squamous cell epithelioma. (2) In a series of basal cell epitheliomas diagnosed clinically as such 15 to 20 per cent will probably prove to be transitional in character. (3) Basal squamous epithelioma, as a rule, is not the result of roentgenotherapy. (4) Basal squamous epithelioma may occasionally metastasize as such, or it may metastasize as a squamous cell epithelioma. Most, if not all, cases of so called metastatic basal cell epithelioma, will prove on microscopic examination, to be basal squamous cell or squamous cell epithelioma. (5) Basal squamous epithelioma is relatively resistant to x ray and radium. Surgical treatment, with an unusually wide excision, is indicated when possible. (6) The prognosis in these cases must be guarded. The tumor is prone to recur.

Warren and associates have described 5 microscopic types and have concluded:

The form of differentiation indicates the degree of malignancy. Differentiation as a basal cell or hair matrix carcinoma is indicative of low malignancy while differentiation toward epidermoid carcinoma is present in the more malignant tumors.

1. *purely ulcerative type* of basal cell growth has been noted in which there is no new tissue piled

up at all. An open ulcer may persist for a long period with no new bulk of tissue occurring, such as one usually thinks of in any neoplasm. Microscopically there is a basal cell solid type of growth with local infiltration by small deeply staining cells, held in abeyance in some peculiar manner as may be seen in some melanomas or common moles in which the cells extend downward without any basement membrane but which for the moment do not spread as a true cancerous growth. This is an insidious growth, because of being easily overlooked until some feature has become widely involved or deep invasion has occurred.

CONCLUSIONS

1. There is a clinical form of basal cell carcinoma that is apparently not very well known and for want of a better term it has been designated clinically as field-fire basal cell carcinoma. So far no distinguishing microscopic feature has been noted.

2. This growth is apt to be misinterpreted as to its true nature and extent.

3. Any basal cell carcinoma is apt to become invasive and the teaching that they are not very dangerous is not correct from a clinical standpoint.

4. The term in alive type might be used more often for more accurate clinical description and for more prompt and extensive attempts at eradication either by operation or radiation. As far as is known, this is a clinical type that cannot be definitely distinguished microscopically except that there is apt to be no differentiation of cells.

5. Basal squamous types have been recognized since Krompecher's original description and may run as high as 20 per cent incidence in supposed pure types.

6. A purely ulcerative stage may exist, with no piling up of new tissue and even with surface healing at times, but with slow persistent deep invasion and widening of ulceration.

7. Basal cell carcinomas give best chance of any carcinomas of cure by early removal, either by excision or radiation but they are definitely more dangerous both for destruction of tissue and life than is generally thought and taught.

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THE USE OF LATEX AND HYDROCAL IN CASTING MEDICAL SCULPTURE

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VISUAL education has become an important factor in the dissemination of medical knowledge. Various forms of medical drawings, photographs, charts, lantern slides, motion pictures, and models have been used to depict anatomical and pathological subjects not easily adapted to or available for clinical demonstration. The realization of a growing demand for new visual methods of presentation has led to the recent development and application of sculpture in making relief models for purpose of obtaining advantages of three dimensional portrayal.¹

The pioneers in this work have been Dickinson and Belski, who have made models of the physiology of conception and labor, and Holt and Falls, working independently, making somewhat similar models of the placenta and intrauterine fetal development. Malvina Hoffman's previous work and advice has been an inspiration and guide to both groups of workers. Recently Holt and Falls have applied their method to the production of models demonstrating pathological subjects such as ectopic pregnancy, premature detachment of the placenta, and cesarean section.² They have illustrated the technique of the low cervical, classical, Porro and vaginal cesarean operations showing the various steps of the actual procedure by means of life sized models and, where necessary, have incorporated instruments.

In order to clarify the discussion of the procedure we are about to describe, it is necessary to distinguish between molding and modeling. According to Frederick—"To model is to construct in some plastic material, as clay, a model which can, if desirable, be reproduced in plaster of Paris,

marble, or similar materials. To mould is to construct in some solid or resisting material, as plaster of Paris, an imprint of an object by means of which a reproduction of the original may be made." Our work was done almost entirely by modeling.

CASTING

For many years physicians and dentists have found impressional casts to be of value when plastic and oral surgery is necessary. For such purposes the making of a cast of the patient's face is purely a mechanical procedure and is usually made before and after surgical operations. In a recent article Peluse has described in great detail this process, using plasticomoulage.³ The negative can be made with agar composition or gypsum and the positives in rubber, wax or any other suitable material. Rubber is now being used for positives such as those for prosthesis of hands, and other artificial parts to be worn to conceal deformities.

The common method of constructing a plaster-of-Paris mold directly over patient's face, whether for normal or pathological masks, has been largely discarded for several reasons, namely, premature separation of positive in mold due to grease used as a separating medium on face, and obliteration, if not loss of skin texture and detail. This method is being replaced by use of a plasticomoulage which is harmless to the skin and can be applied near body temperature, setting almost immediately. The moulage material when hardened is flexible and needs the support of a backing material such as a plaster gauze shell to maintain its shape. This produces a detailed impression or negative. From this a wax positive can be made by the brushing technique which is accomplished by working rapidly and carefully to avoid air bubbles. This can be reinforced by brushing hot wax into a thick layer of gauze laid carefully over first layer of wax. Any defects can be corrected with plasteline. Then a plaster-of-Paris negative is made from this wax working mold and a second positive can then be made successfully of rubber.

The two main substances in common use for making negatives of medical subjects are plaster

From the Illinois State Department of Public Health Division of Maternal and Child Hygiene, the Illustration Studios and the Department of Obstetrics and Gynecology of the University of Illinois, College of Medicine.

¹The illustrations for this paper are photographed from models used as part of a scientific exhibit on "Cesarean Section" prepared as part of the Illinois State Maternal Welfare program, displayed at the annual meeting of the Illinois State Medical Society and the American Medical Association, 1941 and used in undergraduate and post graduate teaching throughout the State.

²Technic of Making Obstetrical Sculpture, demonstrated by Holt and Falls at the mid year clinic American Association of Obstetricians, Gynecologists and Abdominal Surgeons, February 28, 1941, Chicago.

³Peluse S. Arch. Otolaryngol. 1940 31: 955.

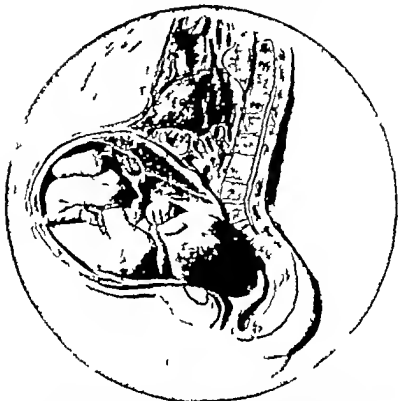


Fig. Tono of full term pregnant woman in labor demonstrating disproportion between normal fetal head and contracted pelvis. The diameter of the fetal head was nearly 10 cm., is 35 feet, and the weight is 50 pounds.

of Paris (gypsum) and a hydrocolloidal compound called agar mold, negocoll, or plasticomontage. Sometimes the wax mold is employed. For inanimate and nonprotoplasmic objects, the rubber and the glue mold are often made. Other substances such as metal, baked sand, terra cotta, korogel, and numerous other materials are used for mold making by commercial manufacturers.

Some materials are more adaptable for casting models than others to accomplish desired results. If properly mixed, plaster of Paris will produce a negative with a great deal of detail. The great disadvantage of its use is the fact that the negative is not pliable and can be used only once because it has to be chipped from the positive and unless this is done with painstaking skill there is great danger of injury to the original.

The most difficult problem encountered in casting is the reproduction of undercuts. An undercut is the space or depression left by cutting the clay away from the edges of the under surfaces of the subject being modeled to increase the third di-

mensional impression. This interferes with the removal from model; therefore, in using plaster it is necessary to prepare piece molds in order to remove the negative from the original clay or the positive from negative where there is any amount of undercutting on a rigid subject.

Glue and gelatin were the first pliable molding materials. They permit large amount of undercutting because the mold will stretch or bend on removal. They both have sufficient elasticity to regain their original shape after having been removed from the cast. Since gelatin or glue and water requires a high temperature for liquefaction for pouring it cannot be used for making a mold directly over living tissue. Moreover it takes a long time to cool which renders it even more undesirable.

Agar composition may be used for the same purposes as glue or gelatin and has the added advantage of not setting until cooled to approximate body temperature; however the latter materials produce stronger and more durable elastic



Fig 2 Model depicting forceps delivery of full term baby during cesarean section. Actual instruments are incorporated and the model was painted

molds. It, therefore, can be applied directly to the skin without damage or discomfort to the patient. Glue or gelatine negatives are damaged by hot wax or other substances which require heat for liquefaction or generate much heat in setting, because heat remelts the mold. Glue or gelatin, therefore, can be used only for plaster casting and



Fig 4 Removing latex negative from hydrocal positive. Edges on surface of negative denote size and depth of undercuts and indicate extreme flexibility



Fig 3 Original clay model on which latex is sprayed to make negative mold. Note number and depth of undercuts

next to rubber offers one of the best methods of molding numerous positive casts from a single negative

MODELING

The first step in making a medical model is for the clinician and the medical artist to discuss in detail the objectives sought in the finished product. If an operation is to be depicted the number of models necessary to clarify the steps of the operation must be determined. The scale of the models must be decided upon—whether they are to be

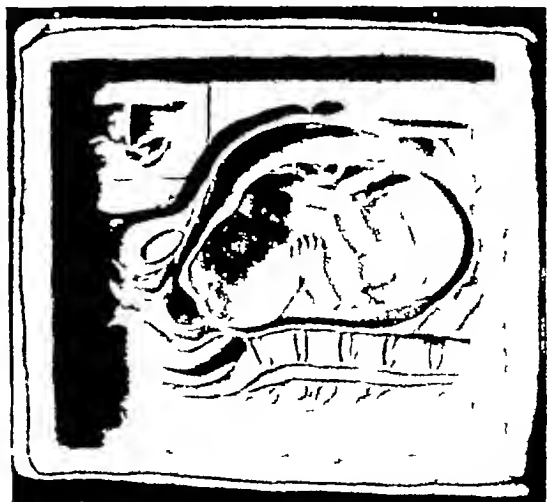


Fig 5 Latex negative backed by plaster of Paris mother mold. Latter shell was applied after complete vulcanization of rubber

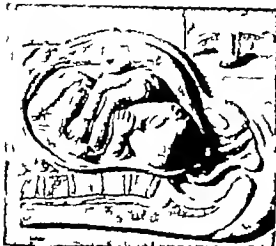


Fig 6 Finished hydrocol positive. Note that the detail in this model is perfect and that retouching or finishing is not necessary. Compare this reproduction with Fig. ure 3.



Fig 7 Hydrocol positive, painted realistically is an insert in upper right corner enhances teaching. The sagittal sections can be done only by sawing; saw coverage cannot be used. Left size model—8 months fetus.

Life size, half or twice scale, etc. The material to be used in the positive and negative casts must be selected, and it may or may not be found advantageous to use impression molds for research in doing the sculpture to produce the best effect. If the models are to be used as exhibit teaching material, it must be decided whether models alone or models supplemented by drawings will be used to illustrate a given subject, since such drawings reduce the necessity for excessive details in models which otherwise would have to be included.

We have found it most practical when possible to have the artist sketch many operations of the type under consideration from life with a free discussion of the steps of the operation with the surgeon before, during and after the operation. A composite picture of the operative procedure is thus obtained by the artist and the clinician is led to observe certain points suggested by questions raised in the mind of the artist. From the sketches each drawing is carefully worked out and criticized and approved by the surgeon who checks anatomical and surgical details. When this has been laid out the actual size it is to appear, it is ready to be transferred or traced on clay. The amount and thickness of clay depends upon the depth involved in the operation or procedure to be reproduced and this determines the type of relief. It is necessary to have adequate armatures to support the weight of clay. The size and detail of model to be rendered determines the amount and type of armature. We have found that broad headed nails which are embedded

in wire meshed hardware cloth are satisfactory for reliefs.

The model of plastiline (oil clay) is rolled out in three dimensional detail as shown in Figure 3 and is now ready for casting.

If these models are made to scale it is desirable to record and reproduce actual anatomical measurements. The necessity of casting numerous undercuts soon made us abandon the plaster negative method and experiment with agar glue and gelatin molds. After considerable research with casting materials, it seemed that liquid latex material had many decided advantages over the others since it has maximum elasticity, is unbreakable, unaltered by hard usage, and is heat resistant. Storage problems are simplified as models can be packed away in small spaces for ready reference and duplication.

Latex is the natural sap of the rubber tree preserved by addition of ammonium up to 6 per cent by volume to prevent decomposition and coagulation. Additional ammonia is added as needed to replace evaporation. It is thermobile and, therefore, must be kept at room temperature.

Materials necessary for making rubber mold are: (1) liquid latex (2) spray gun (similar to one used for insecticides or if available a special DeVilbiss latex compressed air gun) (3) backing and filler compound (4) flat paint brush 1 inch wide (5) spatula for applying backing material and sharp knife for trimming edges of rubber mold (6) bowl for mixing latex and filler compound (7) liquid green soap for cleaning air gun.

and brushes. It is important to note that before the brush is placed in liquid latex, it should be submerged in liquid green soap which is worked into a lather and then wiped off on gauze leaving a thin layer of soap on bristles. This prevents the latex from adhering to the brush. After use the brush should be washed immediately in liquid soap to prevent air vulcanization of latex on the brush. Carbondisulfide can be used as a solvent.

TECHNIQUE OF MAKING RUBBER MOLD

The original clay model is sprayed with a clear lacquer in order to preserve detail, which a brush is apt to destroy, and allowed to dry. The entire surface of the model is then sprayed with liquid latex with special care to reach all undercut areas. The coat takes 30 to 45 minutes to vulcanize by air in a warm room of approximately 70 degrees F and less time in an oven of 150 degrees F. The latter method can be practiced only when a plaster positive is used. It is not suitable for clay which would soften, obscuring detail. Three or four successive coats are applied with a spatula allowing for complete air vulcanization between coats and special attention is given to undercut areas. If the model has deep undercuts, it is now advisable to mix a backing filler with liquid latex to the consistency of a thick paste for the next layer. This is spread on with a spatula, filling in all crevices and depressions solidly to make the mold stronger and more durable. This layer requires a longer period of time for vulcanization and it should stand 24 to 48 hours. When this is hard and firm (especially in the undercut areas) three to five more coats of liquid latex are applied, thus building up the mold to desired thickness, preferably $\frac{1}{8}$ to $\frac{1}{4}$ inch according to size and detail of model. From our experience, it would be well to allow the mold to vulcanize 5 to 8 days, thus giving adequate time to set, thereby preventing undue shrinkage in the negative. The negative shrinks $\frac{1}{2}$ to $\frac{3}{8}$ of an inch over a period of time and if actual measurements are essential this difference should be allowed on original.

When the mold is hard and firm, the edges are trimmed with a knife and the plaster mother mold, which is to serve as a case to support the rubber negative, is made. When dry, the plaster mold is separated from rubber by loosening one corner of the negative and pulling evenly and carefully, it is stripped off like a rubber glove (Fig. 4).

The rubber mold is then washed with water inside and out and placed in the plaster shell, as it appears in Figure 5. The mother mold is now ready for use. The same procedure is carried out for sculpture in the round and is equally simple.

Positive material used may be of plaster or hydrocal, the latter being mixed similar to plaster. However, for best results a soft bristled brush should be used to apply plaster to negative, thereby reducing the chance of the formation of air bubbles in the plaster and insuring sharp detail. Other materials such as resin, wax, compositions, posmouflage, metal, wood, terra cotta, clay, etc., may be preferable.

Hydrocal is a new gypsum base cementation material, discovered by the research department of a large gypsum manufacturer. It has some characteristics of gypsum plaster and some of Keen's cement. It is produced as a dry powder and sets after it is mixed with water. It is characterized by the low amount of mixing water needed, high density, low absorption, high tensile strength and great hardness.

The use of hydrocal is indicated when ordinary gypsum plaster or plaster of Paris is not strong or hard enough. Hydrocal has excellent mixing qualities, settles readily into water, soaks through quickly, and blends to a smooth mix. Setting time is 20 to 30 minutes under ordinary mixing conditions. Four pints of water are used to 10 pounds of dry hydrocal. This amount of mixing water gives a smooth, pourable mix.

PAINTING AND FINISHING MODEL

The model should be thoroughly dry, before it is painted. Small defects may have to be filled in and rough areas smoothed, but it has been surprising how nearly perfect the models come from the rubber mold. After they are removed from the rubber mold they are sprayed with shellac or are boiled in linseed oil, preparatory to painting. They may be finished in a flat color such as ivory, bronze, terra cotta, etc., or painted in natural oil colors. For the purpose of matching colors, we have made a series of color cards corresponding to the colors of tissue seen at operation, recording them with a scale colorimeter in the operating room. Each shade is numbered and numbers of matching shades are recorded on each sketch to assist one in painting realistically.

Success in painting depends largely upon thinness of oil paint and evenness with which it is applied. There should be no "painty" effect or brush marks. Turpentine or linseed oil serve as excellent base mediums. Linseed gives a smooth texture requiring however, a longer period for drying. Sometimes it is advisable to add a bit of Japan drier.

Instruments add to the realism of the model and are embedded in holes provided in the original clay model. After the positive is cast, the instru-

ments are inserted into the grooves and are cemented into place by additional hydrocol. The disadvantage of incorporating instruments is that, during transportation, there is considerable danger of breakage, involving minor repairs.

ADVANTAGES OF LATEX

We have found latex to be far more elastic and pliable than glue and gelatin molds, and the problem of undercuts is solved, for the negative is peeled from the positive cast like a rubber glove and the original shape is resumed. It is stronger and more durable than glue or gelatin, and because of this fact it is possible to produce any quantity of sharp detailed positives, saving time and effort in the long run if duplications are a factor to be considered. The properly prepared mold lasts longer than a glue mold and shrinks less over a period of time. A rubber mold lasts from 5 to 6 years, the approximate life of rubber and can be filed away for future duplication and ready reference.

For many years, rubber in form of dissolved sheet or para-rubber has been used commercially for molding and casting. Such work has proved too technical and involved for average casters and discouraged them for this reason. However latex or natural rubber sap in recent years has greatly simplified the process. It is particularly

favorable because it can be applied without heating and exerts no chemical action on surface in contact. It also vulcanizes by air at room temperature, so that damage to the original model which might follow the use of heat for vulcanization is avoided.

CONCLUSIONS

1. Latex mold is far more elastic and pliable than other molds, thus allowing the casting of deep undercuts without damage to either negative or positive.

2. It is strong and durable withstanding harder treatment than glue or gelatin molds.

3. Latex will vulcanize without heat, but the latter is often desirable to hasten vulcanization.

4. The detail of technique is much more simple and the possibility of error is far less than when glue or gelatin are used.

5. Latex molds are more heat resistant than glue molds which make it unnecessary to remove plaster or hydrocol impression from rubber mold when the plaster warms in setting.

6. The properly prepared mold lasts longer than a glue mold and shrinks less over a period of time.

7. The initial expense of preparing negatives of latex is slightly greater than that of glue or gelatin but the original cost is more than offset by the advantage that unlimited duplications can be made.

THE SIGNIFICANCE OF BLEEDING IN EARLY PREGNANCY AS EVIDENCED BY DECIDUAL BIOPSY

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MOTHER Nature's tolerance of the human reproductive failures would equip her to be the ideal wife of a chronic alcoholic. For too long the human race has believed that once the pleasurable act of impregnation is completed, any subsequent mischance calls for loud lamentations. The old Puritan punished any couple to whom such a calamity befell as having started their family project on the Holy Day—an "iniquitous pleasuring"—until the wife of one of the sentencing justices confounded him. Even today, however, the medical profession manfully strives to maintain the intra-uterine contents far beyond the last metaphysical hope with a necromancy of biologicals and vitamins.

Many and controversial studies of the human spontaneous abortion rate place the "inevitable human wastage" as between 20 and 25 per cent. The percentage throughout the mammalian order runs about 30 per cent of all ovulated or potentially fertilizable ova. If one investigates the expectancy of a successful pregnancy following spontaneous abortion, a certain disbelief of present medical practices is certain to enter one's mind. Malpas, in 1938, beautifully answered this problem. Bradley summarizes Malpas' findings in this fashion:

"At what point in a series of abortions are random or casual factors no longer operable to an appreciable extent? It is manifest that they are still in effect in a series of only two abortions. For example, assuming the rate of spontaneous abortion due to random factors to be 20 per cent, in 100 pregnancies there will be 20 abortions. In the next pregnancy, these patients are still subject to the same rate and therefore 20 per cent of 20, or 4 abortions will occur. And in a succeeding pregnancy 20 per cent of 4, etc. In a large population sample, a certain per cent of abortions will be due to accidental causes, even after 3 or 4 previous catastrophes."

In 6,000 pregnancies which Malpas studied, he found a spontaneous abortion rate of 18 per cent. By an interesting statistical device, he reached the conclusion that chance factors were not ruled out until three successive abortions or stillbirths had occurred. Or, conversely, recurrent factors could not be said to be in operation so that

abortion was habitual until there had been three consecutive failures. In addition, his analysis claims the spontaneous cure rate of abortion to be as follows: 1 abortion—78 per cent will not repeat, 2 abortions—62 per cent will not repeat, 3 abortions—27 per cent will not repeat, 4 abortions—6 per cent will not repeat.

These figures pose the need for revising the term "habitual aborter." One cannot write triumphantly of a small series of cases, in which patients have had one, two, or even three successive abortions, carried to term by what-manner-you-will therapy until the writer corrects his cure rate against the curve of abortion inevitability. By this harsh standard, many successfully treated patients should be reclassified. An 80 per cent cure rate of patients who have had one previous abortion is not phenomenal when 78 per cent of those patients would have carried to term normally without treatment. Bradley suggests that it were far better that habitual abortion as an entity be forgotten, and the terminology be limited to first, second, and third degree, etc., abortion, at least so far as treatment is concerned. In this way, the true problem would be defined and the comparative nature of the successes of therapeutic attempts would not be overlooked.

Again, using our same harsh standards, we must consider the problem of "the pathological ovum." At this point, it is impossible to separate out the pure germ plasma defective ovum from that ovum which, inherently good, undergoes an aberration of development due to defective appendages, poor implantation, local or general causes. We blanket the problem by accepting as a "pathological ovum" one which can be demonstrated either grossly or microscopically as deficient in development. Mall found 48 per cent of his entire collection of abortions were due to this cause. Hertig (4) has found 46 per cent in his series. Mall and Streeter noted that only a fifth of the embryos aborting in the first month were normal, and one-half of those in the second month were normal. In the third and fourth month, eight-ninths of the aborted fetuses had no evidence of pathology. In the latter half of pregnancy, abortions due to pathological ova are found no longer. Monsters

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surviving to term represent an anomaly too slight to cause spontaneous termination of the pregnancy while ova with serious defects involving processes vital to intrauterine growth are aborted early in intrauterine life. One other point worthy of comment is Hertig's (4) finding that 67 per cent of abnormal ova showed signs of hydatid change, while only 11.6 per cent of the normal ova aborted showed this change. Moles were found in 10 per cent of the ova showing hydatid change, and malignancy was found in 20 per cent of the moles.

Hertig (4) in a review of 219 abortions found that 70 per cent of the abortions were due to fetal or placental fault (53 per cent fetal, as defective ova, and 18 per cent defective placental growth or development) and 30 per cent were maternal fault (implantation fault, infection, maternal disease, etc.).

Overwhelmed by this staggering statistical proof of Mother Nature's efficiency in detecting defective fetal development and ridding the womb of such products, the observer is forced to other conclusions. If we accept a 10 to 25 per cent inevitable abortion rate, and if the large majority of those pregnancies are abnormal, what defense is there for treatment which denies a most effective method of terminating unfortunate pregnancies? And, further, how may one select the cases to treat from the bulk of those who should not be treated? At present treatment usually is inaugurated only if the patient complains of uterine cramps, bleeding, or in some instances, a gravid uterus which lags behind the normal growth rate. The patient is given progesterone, vitamins, bed rest, routine sedatives, etc., all or in part, for any one or several of the above signs. Hertig has found that in cases involving a pathological ovum the average abortion date is 10.3 weeks menstrual age, with death of the embryo coming on the average of 6 weeks before the actual abortion is completed (Streeter).

Why continue a pregnancy better to be terminated naturally of an embryo which is not only defective but which has long since ceased in its development? This question emerged quite naturally again and again as a result of the systematic study of all abortions under Dr. Arthur T. Hertig, pathologist of the Boston Lying-In Hospital.

It was such a question which prompted the investigation of this problem. If a safe, easy, accurate, and rapid technique could be developed by which it would be possible to pick out such cases of intrauterine death of abnormal embryos, considerable time, money, and mental anguish could be saved for the patient.

RATIONALE OF TECHNIQUE

We are all familiar with the pathological picture of the decidual cast which is often the only specimen one of these patients will give us. The ovum, with or without the embryo, ruptured or intact, is not always submitted. However, the microscopic picture of an abortifacient apoplexy is well known—consisting of dramatic vascular thrombosis, hemorrhage into the decidua and beneath the placental plate, decidual necrosis, and often an acute cellular infiltration. This is the end-state of nature's catharsis.

In any busy sterility clinic, there are numerous instances of early pregnancies which have been subjected unwittingly to endometrial biopsy techniques, usually without interruption of the pregnancy. Sturgis (1) performed 7 unplanned endometrial biopsies in unsuspected intrauterine pregnancies without the interruption of gestation. This same author (11) described the hypersecretory response which sweeps over the endometrium, completed usually by the end of the eighth week.

We have presented to us, then, the picture of final decidual dissolution as contrasted with the picture of development of normal decidua. Let us suppose a case of inevitable abortion due to be completed at the average of 10 to 12 weeks, with fetal death taking place some 6 weeks before. Fetal death *per se* does not precipitate the abortion, for 6 weeks must elapse before the latter takes place. Does the corpus luteum of this ill-fated pregnancy, aware of its frustration, slowly cease its function, until weeks later the uterus no longer progesterone-inhibited, expels its contents? We have no clinical method for detecting such a blighted ovum. Manual examination in early pregnancy is notoriously unreliable. The biological tests of pregnancy are not dependent upon fetal viability, but upon viability of chorionic villi. If such is the case, then one might well detect the early stages of this "decidual apoplexy" before the actual abortion is completed. A decidual biopsy might reveal these early stages. Such a procedure cannot be defended without clinical evidence suggestive of an abnormal pregnancy such as bleeding, cramps, or failure of uterine growth over repeated examinations.

The biopsies performed in this series of cases were done by means of the blunt-tipped Rock endometrial suction curette and the specimens were put into 10 per cent formalin for immediate fixation. After sterile precautions are observed, the curette was inserted gently under direct view into the cervical canal, and the biopsy tissue was taken from the low anterior uterine wall just

within the internal os, a withdrawal stroke being used. If any resistance was encountered on insertion of the curette, the withdrawal stroke was performed without further forward progress. Since the curette is blunt-nosed, there is extremely little danger that viable membranes will be ruptured or soft tissues will be perforated. It was believed that this information would be of value only in the first 14 weeks of gestation, that after this period the information could be gained by other devices, and the technical risk of taking the biopsy tissue was greatly increased,—not only is the placenta fully formed, but the pregnancy tends to fill more completely the uterine cavity.

Before this technique could be applied to a large group of cases, decidual biopsy was performed on 8 cases in the first 4 months of pregnancy which were to be interrupted therapeutically for maternal medical reasons. Biopsy was performed from 2 to 7 days before the pregnancy was interrupted. In no case were there any symptoms or evidence of harm as a result of the procedure. There have been added to the original 8 cases, 30 more cases, in none of which has there been a casualty. The dangers in the technique will be discussed later in the paper.

The patients who appear in this study were all patients in the Out-Patient Service of the Boston Lying-in Hospital. The patients were entirely unselected, and represent routine study of all bleeding cases. Over an 8 month period, 2,500 prenatal patients were observed to collect 100 consecutive cases of bleeding. In other words, bleeding was present as a symptom once in 25 cases, as the average. These patients were of lower and middle class social strata. They all were desirous of continuing their pregnancies, and in no case was there a hint of induced abortion. Needless to say, the latter consideration aided the study greatly. The majority had had no previous abortions, the most any had was 3 previous successive abortions or 5 in all. Any patient who was in the first 14 weeks of her gestation, who, with or without cramps, had had bleeding of a 5 centimeter spot or greater within the 2 weeks immediately preceding biopsy was subjected to examination of a biopsy specimen after speculum examination had excluded extrinsic causes of bleeding. A patient who had had cramps alone was not investigated. Careful pelvic examination to confirm pregnancy and to exclude ectopic pregnancy and tumors was routine. Two ectopic pregnancies were encountered. Also studied were patients whose wombs failed to increase beyond the size of a 4 months' gestation after repeated examinations over at least a month. The biopsy

specimens were obtained in the Out-Patient Department in the large majority of cases, without the use of anesthetics, and the patients were allowed to go home immediately. No effort was made to quiet the uterus with progesterone or opiates after the biopsy specimens were taken. The patient was encouraged to continue with her ordinary life, or her life was modified according to the information gained from the biopsy material on which immediate frozen section was made. The entire procedure, from the taking of the biopsy material to the making of the frozen section and diagnosis, requires an average time of 15 minutes. There is no special pathological knowledge or technique other than those found in the average, well equipped hospital. Permanent sections stained with hematoxylin and eosin were made to corroborate diagnoses from frozen section, which latter can be prepared for permanent mount as well. The frozen section diagnosis was accurate in at least 90 per cent of the cases, for one's interest is not in delicate cytology, but, as will be explained later, is focused on vascular changes and cellular infiltrations.

The site for obtaining the biopsy material—low on the anterior wall just within the internal os—was chosen as being the least likely spot for implantation of the fertilized ovum. In no instance was the implantation site curetted accidentally. Any subsequent biopsy specimen was taken from a different site so that no pathological changes from the first procedure would obscure the picture.

However, before one believes the microscopic picture from such a small and such a distant site, it must be established that this effectively mirrors the generalized decidual changes, as well as those beneath the placental plate. In the first 6 cases of inevitable abortion turned up on decidual biopsy, differential specimens were taken at the time of spontaneous abortion from the four quadrants of the uterus, from the placental site, as well as from the original biopsy site—low on the anterior wall. From the study of these differential sections, it may be said that if any changes are shown by the original biopsy specimen, those changes will be found throughout the decidua and beneath the placental plate in greater degree. In only one case, to be cited later, was there false security given by a normal decidua, but a repeat biopsy was made a week later which settled the question.

In all, excluding the original 8 patients who were subjected to biopsy in preface to a therapeutic abortion, there were 100 consecutive cases thus examined. Each group will be discussed indi-

vidually. The statistical break-down shows fetal defects, 50 extra fetal defects, 41 nonpregnant, 7 ectopic pregnancies, 3. Of these 100 cases, 18 patients, coming entirely from the 41 whose bleeding was shown to have come from extrafetal defects, have gone on to term. Only 91 cases of the series should be considered true pregnancies, excluding the nonpregnant and ectopic pregnancy cases.

MICROSCOPIC APPEARANCE OF NORMAL DECIDUA

Sturgis (11) as before noted has described the glandular changes and the curve of decidual change found within the endometrium in the early phases of pregnancy. For the purposes of this study the changes within the glands are of less interest than certain other features which will presently be described. In preparation for judging a "normal decidua," 39 cases of decidual specimens from therapeutically aborted patients from the Boston Lying-in Hospital were studied for the features which characterize the decidua and placental plate (chorion frondosum) of early pregnancy. In addition to these cases, were added the original 8 cases of patients with normal pregnancy upon whom the safety of this procedure was checked. Since then 41 more cases with normal decidua have appeared in the series.

In Figure 1 is shown a section of normal cytology. The hypersecretory phase of the glands is an outstanding feature in the first few months of pregnancy but, as Sturgis (11) points out, the height of glandular secretion reaches its peak at 8 weeks, and then slowly fades, until at about 23 weeks the glands have lost their secretory function and have degenerated into large sinusoid-like spaces throughout the spongy decidua.

The endometrial stroma follows a similar course. The localized decidual change about the implantation site spreads slowly until at about 8 weeks, it is found to have reached the lower uterine segment and to have extended throughout the entire endometrial thickness. The biopsy specimen often includes a 1 to 2 centimeter strip of lower uterine segment and endocervix. This is occasionally of interest in dating the time of fetal death, for it will show the arresting of this decidual change in the lower uterine segment. Should unchanged lower uterine segment be found after 8 weeks gestational age, fetal death before that time may be suspected.

Of more interest than the stroma however are the changes one finds in the decidual vessels. This will be elaborated shortly in the description of the pathological changes. In the normal decidua, the arterioles are numerous and prominent

and the decidual sinuses are free of thrombosis.

Last of the significant features of normal decidua is the cellular population found dispersed throughout the stroma. Collections of small round cells, apparently lymphocytes, are found in the stroma, usually as perivascular collections (see Fig. 1) or as subepithelial collections (Fig. 2). Present also may be pyknotic nuclei, possibly of degenerating decidual cells, without cytoplasm, and a certain amount of so called "nuclear dust" of fragmented, degenerated cells. This may be the result of wear-and-tear upon the decidua which has no replacement mechanism for its 9 month existence. These collections are usually in close relationship with the lymphoid elements. Phagocytizing large mononuclear cells are rarely seen. The gland lumina are usually filled with secretion and cellular debris.

The so called moth-eaten degeneration of the deciduiotrophoblastic function which Hertz describes in the decidua of the full term pregnancy has been noted as early as the 1st week of pregnancy and is fairly constant from the 4th month on. This is a hyalinization and vacuolization of the decidua with shrinkage of both apical and cytoplasm. It is of no known significance in this study.

MICROSCOPIC APPEARANCE OF ABNORMAL DECIDUA

To accent heavily the significant changes which follow death of the corpus luteum of pregnancy may Figure 3 be submitted. Here one finds the most marked "decidual apoplexy" for it is the picture presented by sudden complete deprivation of the developing embryo of all the corpus luteum action. Forty-eight hours before, corpora lutea were removed one from each ovary resulting in the expulsion of 17 day normal twin embryos. The pathological picture in the decidua is one of massive acute focal and diffuse necrosis, thrombosis, and congestion of the sinuses, massive hemorrhage into the decidual stroma, and marked acute polymorphonuclear infiltration throughout the stroma. This was a private case and not from the Boston Lying-in Hospital.

To contrast with this, in Figure 4, in which there is slow withdrawal of corpus luteum effect, the thrombosis of the sinuses and hemorrhage into the stroma present, less cellular infiltration—a much less catastrophic panorama. This is the picture more frequently encountered for it apparently is the mechanism of the usual "spontaneous abortion" in contrast to the surgical abortion shown in Figure 5.

And to take this process back even farther one may demonstrate the pathological picture shown

by the abortion of a pathological early villous ovum 8 days after the first missed period (Fig 5, courtesy of Dr Arthur T Hertig) In this, as in 3 other such abortions, all within 4 to 11 days after the first missed period, is demonstrated thrombosis of the decidual sinuses, necrosis of the decidua, hemorrhage into the stroma, as well as deficient vascularization of the trophoblast Undoubtedly, many such cases are missed because the patient or physician does not recognize the specimen Here, abnormal fetal development seems registered almost immediately upon the ovary

The sequence of events pathologically may be reconstructed in this fashion Due to causes which will be discussed later, the corpus luteum of these abnormal pregnancies degenerates at a variable speed, taking an average of 6 weeks, as before noted As the corpus luteum influence is withdrawn, there appear areas of local ischemia due to spasm of the spiral arterioles These areas are diffuse in distribution, but slowly the process becomes generalized, involving the areas beneath the placental plate as well as the entire decidual coat. With the local ischemia comes stagnation thrombosis in the decidual sinuses Often, however, before this can be recognized microscopically, one can find a change in staining reaction of the decidual cell itself—it becomes more acidophilic, and these patchy areas of decidual ischemia are quite prominent by color contrast With tissue death, the demarcation is complete, and there appears extravasation of erythrocytes through the damaged vessel walls into the stroma, with the ultimate appearance of polymorphonuclear leucocytes slowly appearing to aid in separation of the slough In one case, in which biopsy was performed because of bleeding, the first biopsy specimen showed mostly normal decidua with only a fragment of acidophilic-staining decidua The patient was subjected to biopsy again one week later because of continued bleeding and cramps, and 48 hours later, although she was 12 weeks' pregnant by menstrual dates, she miscarried a macerated fetus of 5 to 6 weeks' menstrual age Apparently the first biopsy specimen caught only a fragment of this first patchy decidual degeneration

With the separation of the decidual cast, including the placental plate, where these changes usually are most marked, the patient is ready for the extrusion of this now-foreign body This separation of the decidual coat takes place through the spongy layer A number of these cases were checked by sharp curettage immediately after their abortions, and the curettings revealed

healthy, viable, spongy and basal decidua left behind This process of slow vascular sealing-off, with leucocytic separation of the slough may well be the explanation for the relatively bloodless, noninfected course so many of these patients run Lochia is of a necessity scant, for there is little left behind to slough

In cases of long standing blighted ova, there is often found a "disuse atrophy" of the villi, yet they still are well nourished as long as they maintain contact with the maternal wall

The vascular picture here described in the endometrium is unlike that of anovulatory bleeding, in which thrombosis is found often in the arterioles as well as in the arteriovenous sinusoids Here the picture is one of sinus thrombosis

It may be seen, then, that a frozen section diagnosis is adequate for the large majority of these cases One can detect the difference in staining reaction, the presence of vascular thromboses, and the infiltration of erythrocytes and leucocytes into the stroma On these criteria rests the diagnosis Figure 6 demonstrates an average frozen section of good decidua

DIVISION OF CASES

1 *Fetal defects* Of the 100 consecutive cases studied, exactly 50 per cent have been thrown into this classification No effort was made to distinguish between primary germ plasm defects as opposed to defective development because of other factors Any gross or microscopic abnormality of the fetus or appendages arbitrarily confined that case to this series The large majority of these cases fell into Hertig's (4) average of about 10 weeks' menstrual age as the time for abortion, and the fetal death took place somewhere between 1 week and 4 months, averaging (10) about 6 weeks before the actual abortion transpired No significant alteration of larger statistical studies can be advanced because of the small size of this series The types of pathological ova in general fell into 3 groups those in which the embryo is absent, very defective, or macerated In 58 per cent of the cases embryos were found, in 4 per cent the unruptured ovisac was found, in 16 per cent the ruptured ovisac without embryo was found, decidual cast alone was found in 20 per cent, one hydatid mole was found Hydatid degeneration was noted in 9 of the 50 cases, but no percentages can be recorded because complete specimens were not obtained in all 50 cases

Detailed case history reports will be given on only one case, for it embodies many of the questions which will be discussed later A number of these cases were referred in to this clinic

because of suspected blighted pregnancies, there being one patient who had been given hormone therapy for a 6 month period, despite the fact that the uterus failed to grow beyond the size of a 3 month pregnancy. Others had been treated for shorter lengths of time.

CASE 2. No. 3-4 356. Mrs. I. G., a 35 year old housewife, in 1940 had 4 month miscarriages of unknown cause. Menstrual history revealed cyclical flow every 28 to 30 days, lasting 4 to 5 days, with 2 or 3 pads being used daily. Because of her first miscarriage, she consulted perinat physician who found depressed metabolic rate and put her on thyroid extract. Her last normal period was January, 1941. She had no further menstrual flow, noted breast changes, but no other symptoms or signs of pregnancy. On March 1 she fell on the ice, she spotted slightly. She was hospitalized immediately and given milligrams of prolon (progesterone) intramuscularly for 7 days. During this time she bled pads daily of brownish blood without clots, and was without cramps. She was not examined other than by abdominal palpation. She was discharged after 5 days of bed rest, but was back again 4 days later because of severe cramps of 24 hours duration, during which time she bled pad of bright blood. Over the next 7 days, she bled pads daily of brownish blood, but had no more cramps. She received 50 milligrams of prolon intramuscularly daily during this period. At the end of this time on March 24, 1941 because she still was bleeding, decidual biopsy was performed. The uterus was about half again normal size, the cervix was negative. There was quantity of old blood in the vagina and on, which was a finger tip dilated. A biopsy specimen was taken easily from low on the anterior wall. After the spec was cleaned out, and following the biopsy the patient had no further cramps and bleeding ceased. Pathological examination of the biopsy fragment showed acute necrosis of the decidual fragments, thrombosis of the stroma, and some cellular infiltration. Some unchanged lower uterine segment with hypersecretory glands as also present (Fig. 7). Because of the interruption of the decidual change in the lower uterine segment, it was felt that fetal death had transpired before the 8th week, despite the fact that the patient was by dates to 3 weeks pregnant.

However it was decided to give the patient further trial on hormone therapy, relatively large doses being used, to see if these decidual changes are reversible. As consequence, the patient as given approximately 50 milligrams of progesterone daily for the next 7 days. During the period of therapy the patient felt quite well, she noted no symptoms of pregnancy, she had no further bleeding or cramps. Tissue was then removed from the posterior wall 4 days after the last progesterone, on April 6, just as she again began to flow. Biopsy revealed repeating late secretory endometrium in the lower uterine segment, decidua with vascular thrombosis, cellular exudate, and hemorrhage (Fig. 8). If anything, the decidual picture as worse instead of better after progesterone treatment.

Since it was felt that this pregnancy was doomed, the patient had curettage one day after the second biopsy, on April 7 with yield of scanty curettings of slender decidual pathology with no embryo or appendages recovered.

In all, 6 similar cases were treated with progesterone. No apparent improvement in the decidual picture was found in any of them. From these cases, one may suggest that these decidual changes are irreversible. From a sheer point of

logic, since it is demonstrated amply that fetal death has taken place some weeks before the rationale for using any therapy in these cases is difficult of comprehension. All one does is to delay the inevitable abortion, as evidenced in this case. One case as was mentioned before was carried for nearly 6 months on hormone therapy before it was aborted spontaneously. This latter was a mole.

In several cases, the necrotic slough of the decidual cast could be seen elevated from the underlying endometrium which was in the reparative phase. Such a finding as this would damn any further treatment.

3. *Extrafetal defects.* This group comprised 41 per cent of the cases in the series. Twenty-two of these 41 cases have gone on to viability at least 28 weeks, whereas 19 of them aborted within the first 5 months of intrauterine life. By extrafetal defects, one must suppose that there are no germ plasma defects, but that defects are found in implantation, placentation, or intrauterine maintenance of an otherwise normal fetus. It may be restated that in the 3rd and 4th months, 8 in 9 of the embryos aborted are normal (7/10). Certainly the figures from this small group of 41 cases would bear out those larger series.

The syndrome which evolved on careful study of the normal embryos aborted during the first half of pregnancy is an interesting triad of conditions. Usually the sequence was the premature separation of a low implanted, circumvallate placenta. Several case reports will be presented in detail to adduce this syndrome. Actual digital examination of the uterine cavity was done in those patients in whom abortion appeared inevitable, either from continued loss of blood over a long period of time requiring intervention, or when the os began to dilate under rhythmic spontaneous uterine contractions. If this procedure was not possible because of the stage of labor during which the patient was seen, then the point of rupture in the membranes—determined by postpartum examination of the placenta—was taken as the leading point over the os. Any rupture within a centimeters of the placental margin was taken to be evidence of low implantation of the placenta.

Often the area of premature separation actually could be palpated through the dilated os. Differential biopsy specimens taken in these cases from the area of separation as well as throughout the rest of the uterine cavity showed normal decidua everywhere but in the area of separation where the decidua showed thrombosis, hemorrhage and necrosis (Fig. 9).

Varying degrees of circumvallate formation were found. This finding is not incompatible with an entirely uneventful full term gestation—a frequent finding at routine examination of the placenta postpartum. Hertig (4) mentions this as the etiological factor in 10 per cent of spontaneous abortions. In this series, it was a suggestively frequent finding that at the deciduotrophoblastic junction areas of infarcted necrotic decidua were present (Fig 10). In another case, the site of premature rupture of the membranes was in just such a spot. This may aid in explaining the common mechanism of abortion in the middle trimester, either premature separation of the placenta, or premature rupture of the membranes.

In the series of 41 cases of extrafetal cause of bleeding, the following figures may be submitted: evidence of premature separation was found in 82.6 per cent, low implantation in 60.8 per cent, and circumvallate formation in 32.4 per cent, premature labor in 56 per cent. Hobbs, reviewing the clinical significance of circumvallate placenta, found in 150 cases of circumvallate formation that 22 per cent ended in abortion, 16 per cent in premature labor, with a 33 per cent gross fetal mortality. Painless bleeding was present in 22 per cent. This pointed to the deciduotrophoblastic junction as an area of weakness, predisposing toward hemorrhage with premature labor or rupture of the membranes. The exact mechanism of the abortion, or the eventual fate of the pregnancy, depends upon the summation of these separate fractions. Those patients who went on to term following painless bleeding of varying amounts in early or midpregnancy will be shown to have lesser degrees of these conditions. In a few cases, as will be covered in the evaluation of our study, no cause for the bleeding could be found.

CASE 2 No S-41 393. Mrs B K, a 33 year old house wife with one previous normal pregnancy, 4 years ago. Her periods were regular, every 28 days, lasting 4 days, 1 or 2 pads being used daily. Her last normal period was November 27, 1940. She had no bleeding until March 1, 1941, at which time she began to spot bright blood. This continued almost daily until March 28, 1941, at which time she passed at home painlessly an estimated pint of bright blood with clots. She noted no change in her symptoms of pregnancy. Two days later, while she was in bed, she passed a cup of bright blood without pain. On March 30, she was examined, was found to have no cervical erosion, the vaults were clear, the uterus was 2 fingers below the umbilicus, there was old brown blood in the vagina and in the os. A biopsy specimen was taken from low on the anterior wall without event. Pathological examination demonstrated good decidua. Bleeding remained unchanged after biopsy, and at no time did the patient complain of uterine cramps. However, since she continued to stain 2 to 4 pads daily, she was hospitalized on absolute bed rest. As a test case, she was given 10 milligrams of proluton intramuscularly for

5 days, at the end of which time she was using from 6 to 9 pads daily, the discharge being a brownish blood, and had rare mild cramps. On April 11, because of continued blood loss, and evidence of moderate secondary anemia, it was decided to terminate this pregnancy. The os was 2 fingers dilated. Exploratory finger palpated the placenta low down on the right posterior uterine wall, with the lower edge entirely detached, leaving a free rim of about 1 inch of placenta. Membranes were intact. Differential biopsy specimens were taken from the area of separation and from the other quadrants of the uterus. Section of decidua from the area of separation is shown in Figure 11. Decidua from elsewhere in the uterus was uniformly good. A perfectly normal fetus, consistent with dates, was passed after a Braxton Hicks version. The placenta had been sectioned at the trophoblastic-decidual junction where areas of infarction were present (Fig 10). It was a low implanted placenta, whose lower edge had separated. It was completely circumvallate.

Progesterone had no effect in such a case, for, again, the area of separation showed changes which are difficult to conceive as reversible. One similar case treated with progesterone in the same fashion also failed to improve clinically.

CASE 3 No 3 41-385. Mrs B F, a 38 year old house wife whose first pregnancy, 14 years ago was normal. She had regular flow every 26 to 28 days, flowing 5 to 6 days, using 1 or 2 pads daily. Her last normal period had been November 14, 1940. Pregnancy progressed uneventfully until February 14, 1941, when she complained of cramps, without bleeding, for 1 day. On March 14, 1941, she had cramps with bleeding of 1 pad of bright blood. The cramps stopped, but she continued to flow for the next 10 days, still about 1 pad daily, of bright blood, without clots. The uterus was 2 fingers below the umbilicus, fetal heart was heard, of good quality. There was no erosion of the cervix, vaults were negative. The patient had a biopsy March 28, 1941, without event. The specimen showed entirely normal decidua (Fig 2). The patient was discharged home 3 days after biopsy, and began an active life 1 week later. She continued her pregnancy without event and delivered a 7 pound 14 ounce infant on August 17, 1941. The placenta was completely circumvallate with the membranes ruptured at the placental margin.

This patient might well have benefited from progesterone therapy at the time she was having her uterine cramps without bleeding in the late third month—the so called “critical period” when the placental hormones are replacing the senile ovarian corpus luteum. It is an interesting question—whether an irritable uterus predisposes toward premature separation, or whether defective placental implantation predisposes toward an irritable uterus.

It is of interest that in both of these cases—one requiring interruption because of continued severe hemorrhage, and one with less severe hemorrhage, spontaneously quieting down for ultimate normal delivery—the bleeding began about the beginning of the fourth month. This is near the time when the placenta first begins to exist as a discrete organ, although its function has been established

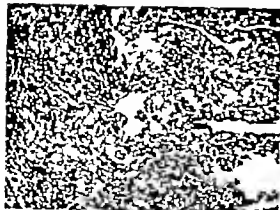


Fig. 3



Fig. 4



Fig. 5



Fig. 6

Fig. 3. Endometrial biopsy from low anterior wall. Thirty-year-old secundipara, 4th cramps and bleeding for days at 4 weeks. Decidua is good, with few perivascular collections of lymphocytes and pyknotic nuclei. Blood vessels are patent. Patient bled no more and delivered a term, healthy infant. Placenta was low implanted.

Fig. 5. Endometrial biopsy from low anterior wall. Thirty-eight-year-old secundipara, 4th 4 weeks' story of intermittent cramps with bleeding. Sections show good decidua, with intact mucosal surface demonstrating subepithelial collections of lymphocytes and pyknotic nuclei. Patient delivered healthy child 1 term. Placenta was completely circumvallate and low implanted.

Fig. 3. Section from spontaneous abortion of normal 7-day 1-m embryo 48 hours after surgical removal of bilateral corpora lutea. Masses infiltration of decidua with polymorphonuclear leukocytes, some thrombi with complete occlusion, necrotic decidua. This represents sudden, complete withdrawal of corpus luteum influence.

Fig. 4. Section from spontaneous abortion of 6 weeks. Fetal death took place at 3 1/2 weeks. Here the picture one of hemorrhage and thrombosis, without marked necrosis or acute exudate. This represents the slow withdrawal of corpus luteum influence by fetal death 5 weeks before.

from implantation of the fertilized ovum onward. It may be that with low implanted or a circumvallate placenta as the more rapid terine growth of the second trimester approaches, this now distinct organ is separated at the margin from the more rapidly growing lower uterine segment. This margin is the already weakened deciduo-chorionic junction. This also is the critical period during which hormone production is shifted.

One case in this group showed hemosiderin deposits within the decidua phagocytes, indicating an old hemorrhage which bore out her history of bleeding at an earlier phase before eventual abortion in the fifth month. The first separation sealed off again and was not too great for continued fetal life. The second hemorrhage continued its retroplacental dissection resulting in complete separation and abortion of a normal fetus consistent with the dates.



Fig 5



Fig 6



Fig 7



Fig 8

Fig 5 Section of a pathological early villous ovum passed 8 days after the first missed period. There is deficient vascularization of ovum, petechial hemorrhage from a sinusoidal rupture, early acute exudate degeneration of the local decidual change. (Courtesy of Dr A T Hertig)

Fig 6 Frozen section of specimen from low anterior wall. Thirty year old primipara with a 1 week story of painless bleeding, uterus slightly behind dates, estimated at 3½ months. Section shows good decidua, with normal physiological lymphocytic infiltration. Two burned-out secretory glands are present, and between them is a patent blood vessel partly filled with free erythrocytes. This demonstrates the important details sought in any biopsy. Three weeks later, the patient had sudden labor and aborted a normal embryo. Placenta was low implanted, and partially circumvallate.

In this group of cases also is the occasional patient who comes in to the hospital well advanced in labor in the early months of the middle trimester. Biopsy tissue taken in these patients, whose stories usually begin either with premature rupture or with premature separation of the placenta will occasionally show focal necrosis

Fig 7 Tissue from low anterior wall. Thirty five year old secundipara with a 2 week story of bleeding with mild cramps at 12 to 13 weeks. Section demonstrates interruption of decidualization of endometrium. On the left is a fragment of necrotic decidua, with an acute cellular infiltration and early thrombosis. On the right is unchanged hypersecretory lower segment endometrium. Decidualization was thought to have been interrupted before the 8th week of pregnancy by death of a pathological ovum.

Fig 8 Specimen from low posterior wall of the same patient 11 days after first biopsy, 4 days after completion of heavy progesterone therapy. Necrosis is more marked, cellular exudate is more definite, some sinus thromboses are seen. Unchanged lower segment also is present in this section, but is not seen in the photomicrograph. There was no reversal of the picture of necrosis on massive progesterone therapy.

throughout the decidua. This necrosis is not nearly as advanced as in the early trimester complete abortion of a pathological ovum, yet it is not within normal limits. This premature degeneration of the decidua would suggest either a relative or quantitative deficiency of corpus luteum hormone. Usually there is so little warn-

ing before either the membranes rupture or severe hemorrhage ensues that treatment cannot be instituted. Since the weight of the evidence suggests that the changes of decidual necrosis are generalized and irreversible. It may well be that no present therapy would avail. If the membranes have been ruptured for more than 24 hours, there is often such a diffuse polymorphonuclear infiltration throughout the membranes and the basal decidua adjacent to the rupture that no valid conclusions can be drawn.

If separation continues to the point of fetal death due to anoxemia, there seems to be good decidua throughout the uterus nearly to the point of actual abortion because of placental maintenance. Usually the bleeding is sufficient to cause intervention but not sufficient to kill the embryo. One is accustomed to the frequent occurrence of difficulty in removing placentas at this stage of pregnancy. However in the occasional case in which the fetus dies of gradual separation of the placenta, the latter slowly undergoes ischemia and fibrosis so that its hormone effects are abolished. Then labor begins, with less difficulty experienced in the separation of the placenta.

3. *The nonpregnant cases*—These cases are included to emphasize the frequency with which such problems are encountered in this clinic. In 7 patients in the series of 100 cases biopsy was done. All of the patients were referred to the clinic because they were thought to be pregnant and possibly were aborting. Only one will be written up in detail.

CASE 4. N. S. 4 386 Mrs. R. H. 4 year old housewife, had been married for 3 years but without issue. Periods are stated to be regular occurring every 31 to 30 days, lasting 6 to 7 days, and requiring one pad daily. Her last normal period was December 2, 1940. She had no bleeding until March 29, 1941, at which time she noted spotting three times in 4 hours following intercourse. She had mild cramps. She had noted pain in the right breast already obese, breast changes, but no other symptoms. She was utterly convinced of pregnancy. On examination the uterus was found to be not enlarged, the cervix was smooth, the vaults were negative. Blood was dark, present in the vagina and in the os without clot. A biopsy specimen was taken from the low anterior wall. Following the removal of this tissue she showed 6 to 8 pads over the next days, and as exhausted and agonized at the thought she was aborting. The pathological diagnosis was a 30 day atypical edematous secretory endometrium. There are no changes to suggest early intrauterine pregnancy but she, as observed for another month, at which time her regular period again ensued. She undoubtedly was not pregnant, but had had a 3 month period of amenorrhea.

It must be emphasized that decidual biopsy material is not suitable as a test for pregnancy. It undoubtedly carries more risk than the biological tests of pregnancy. Unless villi or placental site

giant cells are encountered, one cannot exclude ectopic pregnancy. The finding of either of these would militate against the safety of decidual biopsy. The biopsy material is taken from the lower uterine segment which is not completely transformed into decidua until about the 8th week. Its accuracy must therefore be much lower than the present biological methods. More over Telinde and Henriksen have demonstrated the fallacy of using the finding of decidua alone for the diagnosis of pregnancy. Decidua like changes are possible due to unbalanced corpus luteum rhythm or production, or certain ovarian tumors.

4. *Ectopic pregnancies*—Two such cases are encountered in this series. The finding of decidual necrosis, thrombosed vessels, and eroded in ectopic pregnancy has been described by Mitchell. As in his 2 cases, no harm was done to the patient by the biopsy procedure and the biopsy information when coupled with the clinical stories of the patients made the diagnosis much more secure. In a third case biopsy was done because of a very suggestive clinical history but she was not pregnant, having late proliferative endometrium. This was confirmed by careful pelvic examination and subsequent follow-up. She was transferred to the nonpregnant group of cases already reviewed. The biopsy information aided materially in deciding her case.

5. *Maternal defects*. In the 8 normal early pregnancies in which biopsies were done as controls preparatory to therapeutic abortion, one of the specimens showed an unusual picture. These were patients with severe hypertension, cardiac disease or similar significant maternal disease. The specimen obtained on biopsy from a patient 20 weeks pregnant, a septipara with severe hypertension, showed diffuse and focal necrosis of the decidua with some infiltration of polymorphonuclear leukocytes. It was believed that her vascular system had undergone changes which resulted in diffuse ischemia of the decidua probably through the spiral arterioles—the picture of progesterone lack, but of different etiology. These patients often show acute atheromatous changes within the decidual vessels (3, 14) and not infrequently the fetus dies *in utero* a considerable period before term or premature separation of the placenta occurs. These patients rarely bleed or present bleeding as a symptom, hence do not complicate this study. In an effort to improve the decidual picture and possibly to help in maintenance of its already deficient blood supply the patient was given 20 milligrams of prolonal daily for 7 days, and then a biopsy specimen was taken



Fig 9



Fig 10



Fig 11

Fig 9 Biopsy specimen from area of premature separation of low implanted, circumvallate placenta. Thirty three year old secundipara with a 2 week story of repeated large hemorrhages at 18 to 19 weeks. Decidua from elsewhere throughout the uterus was normal. This specimen shows diffuse polymorphonuclear infiltration.

Fig 10 Cross section of deciduotrophoblastic junction of circumvallate placenta at area of separation in same case. Patient interrupted for continued bleeding despite heavy progesterone therapy. On left are immature villi, next is layer of good decidua, and on the right is focal area



Fig 12

of decidual necrosis with thrombosis, some cellular in filtration.

Fig 11 Section of decidua from area of separation of same case after heavy progesterone therapy. Necrosis is more marked.

Fig 12 Biopsy from low anterior wall. Twenty six year old primipara treated by own physician for 6 months with progesterone for bleeding and cramps at 12 weeks. Specimen shows hydatid degeneration of villi. Twenty-four hours later, the patient passed spontaneously a benign mole.

from the opposite uterine wall. This specimen showed virtually dead decidua, with massive acute exudate, decidual sinus thrombosis, and within the spiral arterioles were the plaques of subendothelial intimal proliferation previously noted as occurring in toxemia, hypertension, and nephritis. This picture was confirmed at the time the patient was surgically interrupted and sterilized. Progesterone in the quantity given was of no avail. The patient had a 1 pound 1 ounce infant which died shortly after birth. The infant

might have died *in utero* within a short time, as suggested by the decidual failure.

As was mentioned earlier, in an effort to determine the allowable changes occurring within the decidua of early normal pregnancies, 59 cases of early pregnancies therapeutically aborted for various reasons were studied. The mothers had nephritis, hypertension, cardiac disease, pernicious vomiting of pregnancy, or other disturbances which conceivably could affect the decidual circulation. These are those same pa-

tients in whom occasionally occurs for no known reason fetal death *in utero* or premature separation of the placenta. Thirty per cent of these cases showed changes within the decidua which we now recognize as characteristic of deficient decidual blood supply but on an entirely different basis than that of the "blighted ovum" or inevitable abortion.

EVALUATION

If one were to emphasize the known effects of corpus luteum hormone they would be (1) initiation of the pregestational changes (2) maintenance of decidual nutrition and thus maintenance of maternal-fetal blood supply, possibly through the spiral arterioles and (3) inhibition of uterine motility. There is no place in this paper for a critical evaluation of the work which has resulted in this now commonly accepted view of the progesterone function. There is no room for discussion of the efficacy of progesterone therapy or vitamin therapy or other present standard forms of therapy. Excellent papers on these subjects are readily available.

Accepting thus the powers of progesterone what is the modus of the pathological picture of the preabortal decidua? We find that in the pathological ovum, which forms the bulk of the abortions in the first trimester fetal death or lack of fetal development due to absence of embryo precedes extrusion by some weeks. Therefore, fetal death must not be directly responsible for kicking off the mechanism of abortion. Fetal death may initiate degeneration of a flourishing corpus luteum of pregnancy. This may come very rapidly as in the cases in which abortion took place within a few days after the first missed period. It may come about very slowly so slowly that one case did not abort for 4 months after fetal death—the *fetus papiraceus* occasionally found years later.

Progesterone works upon different end-organs each of which responds in its characteristic way. The myometrium is inhibited, so that the uterus is relatively quiet, allowing the fetus a calm sea with little ground swell. The decidual development is initiated at first locally by the trophoblast, but as a generalized change is augmented by the ovarian progesterone. The nourishing spiral arterioles are well dilated under progesterone influence. As this influence is withdrawn, the resultant vasospasm, tissue ischemia, etc. result in formation of the decidual slough. When the slough is ready to separate the inhibition threshold of uterine motility is reached, and abortion takes place. Should the expulsive motions

begin before the slough is complete there may be the mechanism of the incomplete abortion with serious hemorrhage. Should the slough be separated and no expulsive movements transpire, there may be the mechanism of the abortus retained for weeks or even months, particularly so if therapeutic corpus luteum is given in the vain hope of continuing the pregnancy.

It appears that the degeneration of the corpus luteum proceeds slowly with the decidual preabortal changes appearing only shortly before the actual abortion, at a time when attention is drawn to the patient because her bleeding either with or without cramps, first calls the problem to the fore. Should the patient bleed from a patch of focal necrosis, biopsy may be misleading unless one perseveres on clinical grounds—as in the case in one patient whose biopsy specimen was normal 5 days before actual abortion. Biopsy tissue taken just before the abortion showed the usual changes.

However the degeneration of the corpus luteum must still remain variable although the average case still requires about 6 weeks following fetal death. One case ended in premature labor 1-3 weeks with a normal decidua and normal fetus. Could this be premature senility of the corpus luteum?

What is the mechanism of premature labor occurring in the middle trimester or of premature rupture of the membranes. Here the corpus luteum should have been replaced by adequate placental manufacture. The interesting triad of findings may be invoked in explanation: premature separation, low implantation, or circumvallate condition.

Yet to be noted are the frequent cases appearing in this mid-trimester group of focal and diffuse necrosis of the decidua, ultimately going on to premature labor. Is this a relative hormonal imbalance or an actual quantitative deficit of progesterone? Is there a lag between the shift from ovarian to placental hormone production. The frequency of focal necrosis at the trophoblastic decidual junctions seems to be of real significance in these cases.

TREATMENT

The help derived from decidual biopsy is definite. In the first trimester it has evolved as a safe procedure which will in the majority of cases indicate the inevitability of abortion. If one finds the so called irreversible changes within the decidua it can be said either that there is fetal death, that there is defective implantation with separation, or that there is serious maternal cause for impairment of decidual nutrition. It

answers immediately the question "Shall further treatment be attempted?"

If one finds decidual necrosis, the chances that the patient will not abort are very poor. In this study, only 1 case of 51 who miscarried in the first trimester had normal decidua. This case not only had normal decidua, but also a normal embryo and placenta—it is pointed out as a possible case for use of progesterone in the treatment of bleeding at this period of pregnancy with a normal biopsy. The case history is against the biopsy procedure's having caused the abortion. The other 50 cases had pathological ova. Six patients with decidual necrosis treated with progesterone went right ahead and aborted, with the decidual picture unchanged or worse after treatment than it was before treatment. The only apparent effect was to delay the inevitable abortion for as long as the hormone therapy was continued. The large majority of these cases had uterine growth much retarded according to dates, definite uterine cramps, evidence of withdrawal of pregnancy hormonal influence (cessation of nausea, breast changes, etc.). These patients can be encouraged to continue normal life until the slough has separated and labor spontaneously begins. This is the safe, easy, relatively bloodless way. Certainly one is not justified in surgical intervention directly the biopsy findings are made known. It is much easier and safer to wait, yet relieving the patient's mind by a simple explanation of nature's protective device for ablating abnormal pregnancies. One is more than justified in refraining from expensive hormone or vitamin therapy, or long invalidism in the futile hope of maintaining pregnancy. A blighted ovum long retained, may require intervention, as may incomplete extrusion of the abortus.

If one finds decidual necrosis, it can mean as well that one has taken the biopsy specimen from an area of premature separation. In this study, only 4 of the 41 cases of extrafetal disease (low implantation, premature separation, circumvallate placenta formation, irritable uterus, etc.) showed decidual necrosis. In the 4 cases showing necrosis, the patients still showed evidence of continued pregnancy, the uterus was consistent with dates, uterine cramps were absent. The bleeding in these cases tends to appear about the beginning of the fourth month, rather than in the second and third month as in the group of pathological ova. It also tends to be bright blood, with clots, whereas the pathological ova cases tend to have dark, brownish blood. Cramps are rarely encountered in these cases.

The finding of decidual necrosis can mean as well severe maternal circulatory impairment. Only 1 of the original 8 cases to be therapeutically aborted bled, presumably from a focal area of necrosis. Since one is not likely to encounter these cases as a biopsy problem, no more mention is made of them as a treatment problem.

If one finds normal decidua in the first 4 months of pregnancy, yet the patient has a story of bleeding, with or without cramps, no definite diagnosis can be made without the careful correlation of clinical story and findings. Thirty-seven of the 41 patients who had extrafetal defects had good decidua. Two of the 4 cases with decidual necrosis aborted, whereas the 2 other cases went on to term. Nineteen of the 41 cases of extrafetal defect aborted with good embryos. Twenty-two carried to 28 week viability. In each of these 2 groups were 2 cases with poor biopsies. In order to settle this quandary, one must follow the clinical course of the patient. If no more bleeding takes place, if the uterus continues to grow, even in the presence of a poor biopsy, one must have curetted an area of premature separation. If the biopsy is good, additional encouragement can be given. If the biopsy is good, but continued bleeding is present, one must follow increase in uterine size. If there continues progressive enlargement, and the bleeding is not devitalizing the patient, pregnancy may be encouraged. Two such cases (already referred to under extrafetal defects) were given bed rest and progesterone without effect upon the bleeding. Both had to be terminated after the bleeding had continued for 3 weeks and anemia had become marked. If the biopsy is good, and bleeding continues, but uterine size is static, too much separation has occurred, and it has been lethal to the fetus. If one follows a case like this by biopsy, he will find soon decidual disintegration as the placental hormones are slowly withdrawn by placental death. All of these variations have been observed. Prediction must be based upon the following. Those who bleed no more with a good biopsy will do well without any treatment other than bed rest, progesterone is given only if there is any suspicion of uterine irritability. If that indication does not exist, there is no proof that progesterone is of any value. These are the cases *par excellence* who are benefited by a routine of limited activity, quiet, sedatives until the separation has stopped and sealing off takes place. One such patient, progesterone treated, with but one episode of moderate bleeding aborted 48 hours after completion of 1 week of 10 milligrams of proluton daily.

In the case of premature labor or premature rupture of the membranes in which focal decidual necrosis (? inadequate progesterone balance) is often found progesterone may be of value but these cases could not be spotted in advance. Usually no warning is given. They silently rupture membranes or suddenly enter stormy labor.

There is no apparent relationship between the amount of bleeding one encounters in the cases of premature separation or other extrafetal defect, and the prognosis for holding the pregnancy. In general, patients who have one isolated episode of a small amount of bleeding have a good prognosis. Biopsy however will settle these satisfactorily in the majority of cases. There is the old rule that if a patient bleeds more than the amount of blood lost in an ordinary menstrual flow the pregnancy will be lost. Several patients have bled as much as several hundred cubic centimeters on several occasions and still have gone on with pregnancy. Others have bled several times monthly until term, never copiously, but enough to keep one on tenterhooks. Others have spotted several times, and then had sudden tumultuous premature labor. It is because of such confusion that biopsy is advanced as a useful weapon in directing intelligent treatment. Continued bleeding of moderate amount over a considerable period of time carries a bad prognosis, particularly if uterine growth stops. Bleeding, matter not the character or amount, is of less consequence in the face of a steadily growing uterus.

It is of interest to note that in the cases of fetal defect the date of average appearance of bleeding is 1.4 weeks after the last period. In the cases of extrafetal defect, bleeding appeared on an average at 9.4 weeks—slightly earlier than in the case of fetal defects. Bleeding in both series in the occasional case would be noted almost from the date of impregnation. In the cases of fetal defect, abortion occurred on the average .4 weeks after the onset of bleeding. In extrafetal defects, abortion took place 8.9 weeks after the onset of bleeding in the average case.

One cause of bleeding shortly after the first missed period has not been mentioned—the so called "placental sign" well known in some of the experimental animals. This is a spotting which is due to a defect in the endometrium at the site of implantation of the ovum (5). It is often thought a period, albeit abnormal, for it approximates the expected date of flow. This may cause some of the miscalculations of confinement. Mention already has been made of abortion occurring within a few days after the first missed period,

possibly a "slightly-delayed profuse period." This may account for the patient's symptoms of pregnancy but for which no subsequent proof can be found.

Morphine is definitely contraindicated in these latter cases, for Falls, Lackner and Krohn found that the postpartum uterus under the usual morphine sedation had enhanced power and frequency of contractions. The barbiturates and paraldehyde are effective agents without morphine's side reactions.

If one were to lay down a plan of therapy to augment as much as possible the natural hormonal processes, one might recommend progesterone just before the time of ovulation and impregnation. Ten milligrams in oil intramuscularly would enhance the normal secretory phase of the endometrium. Just before the 32nd day of the cycle, when implantation takes place another similar dose might be given, as a maintenance dose. No effect would be exerted on the locus of implantation—the hope would be to give the ovum a succulent bed. Since at the time of the first period, there is a slight chance that the fertilized ovum may be extruded, if the improper hormone balance exists, or if it is poorly implanted, a third similar dose might be given just before flow is anticipated. Three cases in the series were so treated following abortion of pathological ova, and all three are now at least 4 months pregnant. No disturbed menstrual thrills were noted following treatment. Obviously no conclusions can be drawn, but if one likes to employ hormone therapy, this is a rationale which may have more effect than the present scheme of therapy. One cannot attempt to give adequate progesterone of foreign source to replace the patient's own deficiencies. At best it is adjuvant therapy.

In the chronic aborter who has had at least three successive abortions, or the low fertility case, weekly injections of progesterone over the first two trimesters may be tried. This is experimental, and would be aimed largely at the problem of decidual maintenance and of quieting of uterine irritability as well as covering the hormone production shift from ovarian to placental source. Many writers have covered this field already. At any stage of pregnancy in which uterine irritability is an annoying symptom, progesterone is ideal. It is impossible to evaluate properly at the moment the "hyperirritable uterus."

One danger of treatment cannot be overlooked. Hertig (4) found, as previously noted, hydatid change in 63 per cent of abnormal ova. Moles were found in 10 per cent of the ova showing

hydrid change, and malignancy was found in 20 per cent of the moles. The one constant cause for malignant degeneration is retention of abnormal or degenerated trophoblastic material. If one injudiciously uses progesterone, and causes retention of such products, there is created a very real danger. One case in this series had a mole. Figure 12 illustrates just such hydrid change in a specimen procured by biopsy.

DANGERS IN THE PROCEDURE OF DECIDUAL BIOPSY

There is a well founded distaste extant for inserting foreign bodies into the gravid uterus. Only 4 patients came to grief, not from hemorrhage, not from infection—neither of these complications was seen a single time. These 4 patients all had blighted ova, proved by subsequent pathological examination by a neutral observer to be pathological ova dead for some weeks. All were within the first 4 months, although one was a blighted ovum, rather Siamese twins of 3½ months, which had been retained for 4 months *in utero*. Membranes were ruptured in these 4 cases because maceration of the intrauterine contents was so complete that the resistance offered by normal viable membranes was not encountered as the curette was introduced. Again, may it be reiterated that no patient had any other untoward effects from the procedure, and that hemorrhage, infection, increased morbidity, or greater tendency toward abortion were not noted in any cases. No perforation is known.

One other source of error in the study was in the interpretation of the early frozen section specimens at a time when the allowable changes within the decidua were still under consideration. These mistakes were corrected by study of the permanent sections, taken as a double check on accuracy. In but 1 case of the 50 pathological ova was the decidual biopsy wrong. This case had been mentioned as such an error before,—a biopsy specimen taken a week after the negative biopsy, 48 hours before abortion, was this time indicative of decidual slough. In the case of biopsy specimens demonstrating good decidua, 7 frozen section diagnoses had to be changed from suspicious to good decidua after the permanent sections were reviewed. This error was not found in the later portion of the study, as greater familiarity with the frozen section details developed. The problems of interpretation of biopsy specimens have been mentioned in treatment.

No biopsy should be performed until all extrinsic causes of bleeding have been eliminated, such as cervical erosion, polyp, vaginitis, and the

like. Actual manual pelvic examination should precede the biopsy to prove pregnancy, if possible, and to exclude ectopic pregnancy or tumors. Needless to say, in a case in which ectopic pregnancy was considered, the patient was in the hospital before the examination was performed. This technique of biopsy is not suitable as a pregnancy test. It is not suited for general use but should be done by one who is acquainted with the usual gynecological biopsy techniques. It is of no value after the 14th week of pregnancy, for the cause of bleeding can be determined by methods less perilous to the gravid uterus, which after that period is well filled by the developing ovum. As with any other procedure, one must weigh biopsy information with the clinical story and physical findings.

SUMMARY

1. An investigation into the causes of bleeding in 100 cases during the first 4 months of pregnancy is outlined.
2. The technique and use of decidual biopsy are described and defended.
3. The histopathological pictures of normal and abnormal decidua are described and the significance of each is elaborated.
4. A general and hormone therapy program is suggested, after exception is taken to present practices regarding bleeding in early pregnancy.
5. Bleeding in the first 4 months of pregnancy in 100 consecutive cases is a significant symptom,—only 22 of 91 presumably normal pregnancies survived to fetal viability after the appearance of this clinical sign.

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A BIOLOGICAL TEST PROPOSED AS A GUIDE IN THE ADMINISTRATION OF THIAMIN

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In 1935 R. R. Williams (5) announced the chemical identification of vitamin B. This substance was given the name thiamin. Williams worked with a concentrate of rice polishings. Shortly after the chemical identification of this substance from natural sources (rice polishings) Williams and Chue (6) were able to prepare the substance (thiamin) synthetically. The synthetic thiamin has been widely accepted as crystalline vitamin B and is said to be as effective as natural vitamin B in the treatment and prevention of vitamin deficiency states.

Many methods have been proposed for guiding the administration of vitamin B and for assaying its quantity in various foods. References to the details of the various methods may be found in the published data of a symposium arranged under the auspices of the Council on Pharmacy and Chemistry and the Council on Foods of the American Medical Association (1). The method detailed in this article is proposed as a procedure peculiarly adapted for the guidance of thiamin administration to patients.

In September 1933, Duhig, of the University of Queensland, Australia, published an article on the serum inhibition of hemolysis. The reason for this inhibition was not apparent. In November 1939, Farley concluded that the administration of thiamin caused the synthesis of a secondary substance in the blood, the amount of which could be quantitated by titrating against digitonin hemolysis the power of inhibition of the serum of the recipient of vitamin B.

The hemolytic systems against which there was inhibition by serum included saponin hemolysis, streptohemolysis, specific amoebocyte system hemolysis, etc. After considerable search it was found that digitonin, one of the saponins, possessed the most desirable properties as a stable hemolytic agent. Hence in the test to be described a standard solution of digitonin is used to study the antihemolytic substance in serum with the idea that the level of antihemolytic power of the serum reflects its content of the substance produced by thiamin. Thiamin itself was found to cause no inhibition of digitonin hemolysis either in watery or serum solution.

From Medical Service A. Pennsylvania Hospital

METHOD

A stock solution of digitonin is prepared by dissolving 80 milligrams of digitonin in 300 cubic centimeters of normal salt solution. For the test 1 cubic centimeter of this stock solution plus 9 cubic centimeters of 0.85 per cent sodium chloride solution is prepared and titrated to establish a factor of complete hemolysis for 0.1 cubic centimeters of a 5 per cent suspension of washed sheep cells. This second solution is called the standard solution. A standard solution of digitonin is freshly prepared and titrated for use on each day that tests are done.

To a series of 10 tubes, the standard digitonin solution is added as follows. 1.0 cubic centimeter to the first tube, 0.9 cubic centimeter to the second, 0.8 cubic centimeter to the third, 0.7 cubic centimeter to the fourth, and so on, decreasing the volume by 0.1 cubic centimeter until the last tube contains 0.1 cubic centimeter. Salt solution is then added until the total volume in each tube is 1.0 cubic centimeters. To this, 0.1 cubic centimeter of a 5 per cent suspension of washed sheep cells is added. All tubes are incubated at 40 degrees C. in a water bath until no further hemolysis occurs. This usually takes about 3 minutes. The last tube showing complete hemolysis is considered the factor or the amount of digitonin solution to be used in the test. The serum to be tested is diluted 1:1000 in 0.85 per cent sodium chloride solution. Eleven tubes are set up, and to the first 10, beginning with 1.0 cubic centimeter of serum dilution in the first, the amount is decreased by 0.1 cubic centimeter until the tenth contains 0.1 cubic centimeter. Tube 11 is the control, containing no serum. Digitonin standard solution, the amount determined by the previous titration, is added to each tube and normal salt solution is added to make 1 cubic centimeters in each tube. To each tube 0.1 cubic centimeter of a 5 per cent suspension of washed sheep cells is then added.

The tubes are incubated at 40 degrees C. until hemolysis is complete in the control. (This usually takes about 3 minutes.) The test is read immediately after the control shows complete hemolysis. The dilution values read refer to the original dilution of the serum in 1.0 cubic centi-

meter and are not based on the total volume of 22 cubic centimeters. This is done because of greater ease in reading and because the comparative power of the serum of patients to inhibit is desired.

Readings The tubes showing complete inhibition of hemolysis, i.e., the end point, constitutes the reading on the particular serum being tested. Instead of reading the end point as a dilution, it is assumed that the dilution contains the number of units corresponding to the last figure of the dilution, for example, a serum which inhibits hemolysis in a dilution of 1:1000 is read simply as 1000.

Rationale of proposed test An original observation was made that individual blood serum varied widely in its power of inhibiting hemolysis. A search was undertaken for the explanation of this phenomenon. Attention was directed to the vitamin content of serum as a possible explanation. It was found that yeast, which had been autoclaved for 6 hours, when fed to rabbits caused no rise in serum inhibitory power of their serum. When unautoclaved yeast was used to feed the animals, a rise in serum inhibitory power occurred. At this point it was noted that the yeast being used was a commercial product to which thiamin had been added. Yeast to which no thiamin had been added was obtained. When this yeast was fed to rabbits the rise in inhibitory power was not spectacular as it had been in the artificially thiaminized yeast. Attention was, therefore, focused on thiamin. A small dose of thiamin chloride (1 milligram 3 times a day) was taken by the experimenter for 1 week. At the end of 1 week the titer of his serum had risen from 5000 to 100,000. After an interval of several weeks, with the return of titration of his serum to 5000, the same individual took 6 milligrams a day for 1 week, with a rise in the titration of his serum to 350,000. It was thought that thiamin not only caused a rise in the inhibitory power of the recipient's serum, but also that this rise was quantitative and that the height of the rise depended on the amount of thiamin given.

EXPERIMENTS ON RABBITS

Rabbits were given varying amounts of thiamin. A rise in the inhibitory power of the rabbit's serum invariably occurred regardless of whether thiamin was given by mouth or by injection, subcutaneously or intravenously. There was usually an interval of 2 or 3 days before the rise began. Rabbits given a relatively small dose of thiamin, 3 milligrams daily for a week, showed at the end of that time a serum titer of about

100,000, whereas the initial titer of their sera was, for example, 1600. The degree of rise in titer appeared to depend upon the amount of thiamin used. The massive dosage used in the experiments quoted was to illustrate the spectacular effect of a large quantity of thiamin. The rabbits appeared to suffer no ill effects from the large dosage used. (Table I)

TABLE I—RESULTS

Group A Administration hypodermically, 50 milligrams daily for 1 week

Rabbit No	Preliminary titer	Titer after 1 week
1	1250	1,000,000
2	1600	500,000
3	1000	500,000
4	500	330,000
5	1500	500,000

Group B Administration intravenously, 50 milligrams daily for 1 week

Rabbit No	Preliminary Titer	Titer after 1 week
6	1200	5,000,000
7	650	3,000,000
8	1050	3,000,000
9	1550	2,500,000
10	1600	5,000,000

Group C Administration intravenously, 50 milligrams daily for 1 week

Rabbit No	Preliminary titer	Titer after 1 week
11	2000	1,450,000
12	1450	2,500,000
13	500	3,300,000
14	1450	5,000,000
15	2000	5,000,000

Group D Administration hypodermically, very massive doses—100 milligrams daily for 1 week

Rabbit No	Preliminary titer	Titer after 1 week
16	1250	10,000,000
17	1000	10,000,000

Group E Administration by mouth, 6 milligrams daily for 1 week

Rabbit No	Preliminary titer	Titer after 1 week
18	500	90,000
19	500	90,000

CONTROL ANTICHEMOLYTIC EXPERIMENTS ON RABBITS WITH SUBSTANCES OTHER THAN THIAMIN

Obviously it was difficult to control the possibility that substances other than thiamin, when given intravenously or by mouth to animals, might also cause a spectacular rise in the inhibitory titer of the serum of the recipient. This was true because many vitamins have not been

isolated and therefore are not available and there is no limitation to the number of other substances which might be used. Therefore, four unrelated substances were selected, one a vitamin of the so called water soluble vitamin group a second possessing vitamin like activity the third a product with a high protein content and the fourth a substance commonly used to produce therapeutic shock.

Typoid vaccine, massive doses intravenously for week. Results: There was slight rise in the antihemolytic power of the serum of the recipient, but in no way comparable with that given by thiamin.

Nicotinic acid, large doses by mouth for week. Results: No rise of inhibitory power of the serum of the recipient.

Casein, large doses by mouth for week. Results: No rise of inhibitory power of the serum of the recipient.

Vitamin C; ascorbic acid, large doses intravenously for week. Results: The inhibitory power of the serum showed no rise.

With the four substances used there was no marked rise in inhibitory power of serum of the recipient against digitonin hemolysis.

RESULTS OF TITRATIONS OF SERA FROM HUMANS

Many titrations on the sera of humans have been done. The results of titrations of the sera of 345 individuals are shown in Table II.

TABLE II

Number of individuals	Diagnosis	Average titration	Maximum titration	Minimum titration
	Pneumococcus lobar	1,800	3,000	300
30	Asthma-bronchial	1745	3000	150
	Diabetes mellitus	2000	1,000	1000
10	Moderately advanced to advanced carcinoma	1,300	300	3000
100	Pregnancy	157	300	1000
	Pellagra	800	150	30
	Active rheumatic heart disease	1744	300	1000
	Cerebral sclerosis	300	1,000	1,500
	Myasthenia gravis	1000	1000	1000
	Carcinoma of liver	300	300	1,500
100	Variable	7	3000	1000

Of the individuals suffering from bronchial asthma listed in Table II 23 of 30 cases showed a titration below 1,000 of the cases of lobar pneumonia, 24 of 46, of diabetes mellitus, 4 of 2 of carcinoma, 1 of 20 of pregnancy 13 of 100 (4), of rheumatic heart disease active, 13 of 23 of coronary occlusion, 2 of 8 of cirrhosis of liver 2 of 3.

Analysis of the tests on sera from diseased individuals failed to show a consistently low inhibitory titer in any one disease. There was, however, a marked variation in inhibitory titer of the sera of diseased persons.

The average of tests on the sera of 100 presumably normal individuals was 1,712. The sera of 98 per cent of these showed a titration between 1,000 and 3,000. Eighty nine per cent were between 1,000 and 1,500. We assume therefore that the minimum normal is 1,000. In other words titrations below 1,000 are considered by us to be deficient in the inhibitory substance following thiamin administration. The 100 individuals were young men and young women, either student nurses or medical students. All were in good health as far as could be determined by ordinary history and physical examination. Their diet consisted of that ordinarily selected by each. In the case of the student nurses, this was the hospital diet given to such individuals. No attempt was made to supervise such diet as to its vitamin content, as the object was to learn what would be the inhibitory titer of the sera of such individuals on an unselected diet. There was no apparent difference between the sera.

RESULTS BEFORE AND AFTER THIAMIN ADMINISTRATION

Following are details of the findings in some patients who had been on a low vitamin B₁ dietary intake before admission to the hospital with the results of their serum inhibitory titration before and after treatment by thiamin.

CASE 1. H. R. aged 42 years, diagnosis, pellagra, anorexia, stomatitis. Patient had been on milk for 3 years and had lived on an inadequate diet consisting largely of bad bakery known locally as goshers, and potatoes. Before treatment the inhibitory power of the sera was 150. He was given thiamin chloride in capsules daily by mouth, also ascorbic acid. (We have found that ascorbic acid causes no rise in inhibitory power.) He is given high calorie diet. The effect of this on the inhibitory power can not be exactly calculated. After 5 days his serum titer was 3,000 and his symptoms of diarrhea and skin eruptions were greatly improved.

CASE 2. H. C. aged 38 years, diagnosis, tuberculosis and pleural effusion, occupation, stenoclone. Patient had suffered from poor appetite with marked limitation of food intake and loss of 5 pounds in eight or a period of 6 months. Before treatment his inhibitory power was 30. He was given thiamin chloride in capsules daily by mouth, and high calorie diet. After 10 days his inhibitory titer was 1,500.

CASE 3. P. C. aged 58 years, diagnosis, advanced liver occupation, shoestring salutarin. For 3 years before admission to hospital he had been living on a diet of 30 cents a day for food. Inhibitory titration before treatment was 150. He is placed on thiamin chloride in capsules daily and high calorie diet with strict supervision. 7 days in his titration was 1,000, to days later 3,000.

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INGUINAL HERNIAS

IF we accept the theory of Professor Ernest Hooton in his book *After Men and Morons* we may expect to find more hernias today than ever before. He wrote

With the development of urban civilization and industry physical deterioration becomes appallingly common every sort of physical abnormality is increasingly prevalent. The expanding mechanization of this age however with the use of labor saving devices in home, field, and factory should favor a reduction of hernias, which might offset the physical deterioration of civilized man mentioned by the distinguished anthropologist.

Some notion of the incidence of hernias can be gained from figures furnished by the selective service examination boards. In 1917 and 1918, out of more than two million men examined for the draft, 4 per cent showed either a hernia or enlarged inguinal rings. Among the present draftees, 1.8 per cent of the million men so far examined have been rejected because of the presence of a hernia.

The somewhat lower percentage of hernias in the men now being called for army duty is not a reliable measure of the actual number of such defects in the entire population. The draftees are young men. Hernias show a marked tendency to increase in frequency with age, and the lengthening of the average life cycle has resulted in an increased number of older persons in our population. We must infer therefore that in a study including all age groups a higher percentage of hernias would be found than that expressed in the figures from selective service examinations.

Statistics from life insurance companies and the United States Public Health Service indicate that the incidence of hernia in the general population has not varied much in the past thirty years.

On the basis of such meagre reliable data as is available today however the most careful biometrician could not offer us any final judgment as to whether hernias are becoming more or less prevalent.

About 10 per cent of the surgery of the large general hospital is devoted to the repair of hernias of all types. Approximately 90 per cent of these are of the inguinal variety. The recent increase in the number of inguinal hernias operated on can probably be attributed, at least in part, to the fact that most states have put into effect some form of workmen's compensation laws in the past few years. These laws have so placed the responsibility of the employer that he has found it wise to have every prospective employee examined before he begins work. Men who are found to have hernias when they seek employment must have them repaired in order to be accepted for the position.

Surgical correction, when expertly done,¹ offers the most reliable form of treatment of these congenital or acquired defects. The methods of repair have changed very little in the past fifty years. Such slight variations and modifications of the early operations of Bassini and Halsted as have been introduced have probably had little influence on the success of herniorrhaphies. The most outstanding innovation, namely the use of autogenous fascia, was first described by McArthur in 1901, but recently it has enjoyed an increased popularity. There is a good deal of discussion and difference of opinion at the present time as to its true value, some men presenting statistics to show that its use will greatly lower the incidence of recurrences and others giving figures to show a large percentage of failures, even when fascia is routinely employed. It would seem that its greatest value lies in bridging structural defects which are common to the direct hernia and which exist in only a small measure in the indirect type of inguinal hernia.

Another era of enthusiasm for the injection treatment of hernia is just quieting down. During the past five years certain members of the profession have rejuvenated this early method of treatment until it has attained a considerable vogue. Its rather extensive use has yielded but few crumbs of comfort for its sponsors. It has been found to be serviceable in only a limited number of cases, and when it has been employed without a careful selection of patients, the very high percentage of failures has aroused a skepticism of its usefulness that is fully warranted. The most that can be said for the injection treatment of hernia is that its field is limited and its permanent successes few.

The profession was rudely startled rather recently by reports from surgical centers that the incidence of recurrence in direct hernias

was as high as 20 to 30 per cent. Most statistical studies on indirect hernias report a recurrence rate of 3 to 7 per cent.

It must be kept in mind that in the direct hernia we are dealing with a gradually developing structural breakdown. Bodily reparative processes are at a low ebb, and hence the success of ingenious methods of repair is curtailed both by the inadequacy of the body and by the dearth of satisfactory tissue to be used in closing the defect.

It is lamentable that many surgeons of this age are inclined to devote less and less study to the anatomy of the inguinal region and to the understanding of the basic structural factors which cause a hernia. Therefore, they cannot be as well prepared to deal with this condition as were the anatomist-surgeons of a few years back.

Because the younger generation tends to neglect the foundations essential to an intimate knowledge of this problem, a renewed interest must be periodically stimulated. Too often today a hernia repair is not considered of enough importance to merit enthusiastic study. It comes to the attention of many older surgeons that their young colleagues not infrequently are working at a great disadvantage because of their lack of fundamental knowledge of the structures they are attempting to repair. Those who are called upon to perform herniorrhaphies must be familiar with the anatomical relations of the normal parts and the changes in anatomical arrangement which take place with the appearance of a hernia. Even before intraperitoneal surgery was attempted, there were many accurately descriptive and beautifully illustrated texts on the repair of hernia. The anatomist-surgeons, who were pioneers in this field, with meticulous care prepared atlases of anatomy which residents and fellows in surgery today would do well to study diligently. Before these young

men give too much of their time to newer and possibly more dramatic developments in the surgical field, they should see to it that they are fully conversant with the problems of hernia repair.

It behooves us then, to put more stress on the thorough training of our medical students in the anatomy of these regions and in the understanding of the structural factors causing a hernia.

RAYMOND W. MCNEELY

THE NEED FOR TRAINED PERSONNEL IN ARMY DEPARTMENTS OF PHYSICAL THERAPY

IN the modern military hospital the department of physical therapy plays an important part. Traumatic lesions commonly encountered in military practice often require physical treatment during the stage of rehabilitation. During the last war it was estimated that 50,000 to 75,000 reconstruction cases would be received per year from each 1,000,000 men overseas and by June 1919, there were forty-five officers, fifty-four enlisted men and 700 reconstruction aides devoting their time to physical therapy.

At the present time there is an extreme shortage not only of physical therapy physicians, but also of physical therapy technicians (physical therapy aides). It has been estimated that 300 physicians and more than 2,000 physical therapy aides will be needed in military hospitals. At present there are in this country only about 1,600 qualified physical therapy technicians to take care of civilian needs. There was a shortage of such workers prior to the war and since Pearl Harbor the need for trained medical specialists and trained technicians in physical therapy has become extremely acute.

Plans have been developed for the training of a certain number of medical officers to con-

duct military physical therapy departments, and a number of schools for physical therapy technicians are in existence. The great need at the moment is to obtain a sufficient number of qualified students for both courses. The Surgeon General's Office is now assigning active and reserve medical officers interested in the subject of physical medicine for special training in the field and any medical officer who is interested in such training should consult the Office of the Surgeon General. The physician who is not a reserve officer and who desires such service should make application for it through Procurement and Assignment Service for Physicians, Washington, D. C.

The technicians who are being trained in emergency courses should now be drawn from the schools for physical education throughout the country and from the colleges of liberal arts. The Army has expressed its preference for female physical therapy aides, and any young woman who is a graduate of an approved college of physical education or who has had two years of academic college work, including courses in physics and biology in an approved college is eligible for admission to most of the approved schools for physical therapy technicians.

The young women of the country who are desirous of serving their country and who have the training which has been mentioned should be urged to communicate with the nearest school for physical therapy technicians and attempt to receive the necessary training in order that they may serve this tremendous need. In a recent official communication appears the following statement: "With the great expansion of the Army and the paucity of the required number of Physical Therapy Aides, something must be done and must be done immediately. The schools for physical therapy technicians which have been approved by the Council on Medical Education

and Hospitals of the American Medical Association and which, therefore, are the only ones which are acceptable to the Office of the Surgeon General are as follows

Name and location of school	Medical director	
Children's Hospital, Los Angeles, California	Steele F Stewart, M D	Hospital for Special Surgery, New York, New York
Stanford University, Stanford University, California	W H Northway, M D	D T Watson School of Physiotherapy (affiliated with University of Pittsburgh School of Medicine), Leetsdale, Pennsylvania
Walter Reed General Hospital, Washington, District of Columbia	B A Strickland, Jr, Capt, M C	College of William and Mary, Richmond, Virginia
Northwestern University Medical School, Chicago, Illinois	John S Coulter, M D	University of Wisconsin Medical School, Madison, Wisconsin
Bouve-Boston School of Physical Education, Boston, Massachusetts	Arthur L Watkins, M D	University of Minnesota Medical School, Minneapolis, Minnesota
Harvard Medical School, Boston, Massachusetts	Frank R Ober, M D	
Boston University, Sargent College of Physical Education, Cambridge, Massachusetts	Louis Howard, M D	
Posse Institute, Kendal Green, Massachusetts		
Mayo Clinic, Rochester, Minnesota	Frank H Krusen, M D	
St Louis University School of Nursing, St Louis, Missouri	Alexander J Kothis, M D	
University of Buffalo School of Nursing, Buffalo, New York	George G Martin, M D	

The schools listed are equipped to train students in physical therapy, and they must receive an adequate supply. In one of the civilian institutions of this country, approximately a twelfth of the total number of patients receive some form of physical therapy, in army hospitals, the percentage of patients is even higher. For example, it has been estimated that at the Walter Reed General Hospital in Washington, D C, approximately a fifth of all the patients who are admitted receive some form of physical treatment. It is imperative that these needs be met.

FRANK H KRUSEN

THE SURGEON'S LIBRARY

REVIEWS OF NEW BOOKS

IN modern English or American literature there is no other encyclopedia of epilepsy which treats the subject so completely, concisely, and yet simply as does *Epilepsy and Cerebral Localization*. The authors, particularly the senior author, are recognized authorities in their subject, and not only have they drawn upon their own clinical material and experience, but they have freely used recent and as yet reliable data from many other important sources. The title of the book should not overawe any physician. While it is indeed a scholarly treatment of an evasive subject, yet in no wise has it been prepared solely for the intellectually elite. It is a practicable, readable book, so arranged as to subject matter that each topic is broken down into simple components, discussed to the point of clarity without overall detail, and freely enlivened by a well selected choice of clinical illustrations.

Many commonly used expressions and names of epileptiform phenomena are defined with simplicity, especially in Chapter IV dealing with "Seizure Patterns." The authors believe that in the strict sense of the word there are no extracerebral causes of epilepsy which disease they define simply as "an excessive or abnormal neuronal discharge." They do believe that various extracerebral disease states may cause epilepsy through interference with cerebral circulation or through an effect on cerebral metabolism or function.

A long and well written chapter on the use of electroencephalography by Herbert H. Jasper is included. Recognizing the rapidly changing status of this diagnostic procedure the author ventures to state that the electroencephalogram cannot be depended upon to give a certain diagnosis of clinical epilepsy without the aid of other data, and, therefore, no single pattern of electrical activity of the brain which is pathognomonic of that usually considered an "idiopathic" disorder.

The chapters on the various forms of treatment, including the authors' surgical methods, are useful

to the physician directly concerned with his own epileptic patients. The relative merits of bromides, phenobarbital and dilantin, together with many other forms of medical treatment, are presented. The discussion of surgical treatment labelled with reserved brevity, indicates the success and failure to be expected by such therapy as exemplified by the large epilepsy series of the Montreal Neurological Institute. The intelligent and successful management of the epileptic man or woman as a member of society (which more likely than not is void of understanding and tolerance) is a final test of one's ability to treat the epileptic state.

JOSEF MURPHY

APPROXIMATELY fifty per cent of patients have no demonstrable physical findings or signs but are all complainants or symptomatic. With increased emphasis upon the pathogenesis of disease and with advances in the uses of laboratory procedures the value of the interpretation of symptoms has been underestimated.

In *Symptoms in Diagnosis* the author gives his attention to symptoms encountered in clinical medicine. An attempt is made to be comprehensive. The book is not profound and contains nothing new. On the contrary symptoms are interpreted in a concise and practical manner but in the light of recent scientific and clinical knowledge. Its clarity and brevity makes it easily usable.

The chapter on disturbances in sensation is of particular value and well presented. Here the author is presenting the commonest and often the most elusive symptoms with good clinical sense. Exceptions might be taken to some of the views expressed. For example in discussing pericardial pain it is stated that, "pain due to pericardial lesions is localized to the pericardium."

This book will be of greatest service to the student of physical diagnosis. To the clinician it will serve as stimulus to analyze more carefully the symptoms presented by the patient.

HOWARD B. CARROLL

EPILEPSY AND CEREBRAL LOCALIZATION: A STUDY OF THE MECHANISMS INVOLVED IN THE PRESENTATION OF EPILEPTIC SEIZURES. By Walter F. Floyd, L.B.S., M.D., D.Sc., and Theodore C. Lowenstein, M.D., M.Sc., M.D. Ph.D. Springfield, Ill. and Baltimore, Md. Charles C. Thomas, 1943.

SYMPTOMS IN DIAGNOSIS. By Jonathan Campbell Macklin, M.D. L.L.D. Boston, Little, Brown & Co., 1941.

